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L42 56 L35 AND (PY<2003 OR AY<2003 OR PRY<2003)

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YOU HAVE REQUESTED DATA FROM 56 ANSWERS - CONTINUE? Y/(N):y

L42 ANSWER 1 OF 56 CAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 2008:10367 CAPLUS <<LOGINID::20080505>>

DOCUMENT NUMBER: 148:93277

TITLE: Histone deacetylase inhibitors for treating degenerative diseases of the eye

INVENTOR(S): Hellberg, Peggy E.

PATENT ASSIGNEE(S): Alcon, Inc., Switz.

SOURCE: U.S. Pat. Appl. Publ., 8pp., Cont.-in-part of U.S. Ser. No. 694,309.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| US 20080004311 | A1 | 20080103 | US 2007-836309 | 20070809 <-- |
| US 20040092431 | A1 | 20040513 | US 2003-694309 | 20031027 <-- |
| CA 2504226 | A1 | 20040527 | CA 2003-2504226 | 20031027 <-- |
| AU 2003286686 | A1 | 20040603 | AU 2003-286686 | 20031027 <-- |
| EP 1562592 | A2 | 20050817 | EP 2003-777895 | 20031027 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003016163 | A | 20050927 | BR 2003-16163 | 20031027 <-- |
| JP 2006508120 | T | 20060309 | JP 2004-551572 | 20031027 <-- |
| US 20070088045 | A1 | 20070419 | US 2005-531747 | 20050418 <-- |
| MX 2005PA04738 | A | 20050803 | MX 2005-PA4738 | 20050503 <-- |
| IN 2007DN07459 | A | 20071109 | IN 2007-DN7459 | 20070927 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-425576P | P 20021112 <-- |
| | | | US 2003-694309 | A2 20031027 |
| | | | WO 2003-US33873 | W 20031027 |
| | | | IN 2005-DN2543 | A3 20050613 |

AB The invention discloses compns. and methods for treating degenerative conditions and diseases of the eye with histone deacetylase inhibitors.

IT 149647-78-9, SAHA

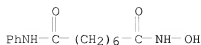
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(histone deacetylase inhibitors for treatment of degenerative eye diseases)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; histone deacetylase inhibitors for treatment of degenerative eye diseases)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L42 ANSWER 2 OF 56 CAPLUS COPYRIGHT 2008 ACS ON STN
 ACCESSION NUMBER: 2007:705011 CAPLUS <<LOGINID:20080505>>
 DOCUMENT NUMBER: 147:125824
 TITLE: Controlled release solid oral dosage form containing a histone deacetylase inhibitor and a medium chain fatty acid derivative as an absorption enhancer
 INVENTOR(S): Cumming, Kenneth I.; Ramtoola, Zebunnissa; Leonard, Thomas Waymond
 PATENT ASSIGNEE(S): Merriam Research I Limited, Ire.
 SOURCE: U.S. Pat. Appl. Publ., 35pp., Cont.-in-part of U.S. Ser. No. 510,560.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-----------------|
| US 20070148228 | A1 | 20070628 | US 2006-450641 | 20060609 <-- |
| US 20030091623 | A1 | 20030515 | US 2000-510560 | 20000222 <-- |
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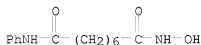
AB The invention relates to a pharmaceutical composition and oral dosage forms comprising an histone deacetylase (HDAC) inhibitor in combination with an enhancer to promote absorption of the HDAC inhibitor at the gastrointestinal tract cell lining. The enhancer is a medium chain fatty acid or a medium chain fatty acid derivative having a carbon chain length of from 6 to 20 carbon atoms. Preferably, the solid oral dosage form is a controlled release dosage form such as a delayed release dosage form. Thus, granules comprising 61.05% parnaparin sodium, 33.95% sodium caprate and 5% polyvinylpyrrolidone were prepared and administered orally to humans. The mean delivery of parnaparin, as measured by plasma anti-factor Xa levels, was considerably higher from the solid dosage form than that from the corresponding solution dosage.

IT 149647-78-9, Suberoylanilide hydroxamic acid 382180-17-8
 , Pyroxamide 537049-40-4, Tubacin
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (controlled release solid oral dosage form comprising a histone

deacetylase inhibitor and a medium chain fatty acid derivative as an
absorption enhancer)

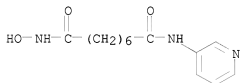
RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



RN 382180-17-8 CAPLUS

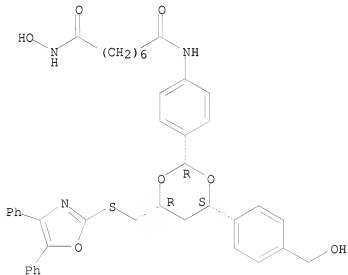
CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



RN 537049-40-4 CAPLUS

CN Octanediamide, N1-[4-[(2R,4R,6S)-4-[[4,5-diphenyl-2-oxazolyl]thio]methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N8-hydroxy-, rel- (CA INDEX NAME)

Relative stereochemistry.



IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitor; controlled release solid oral dosage form comprising a histone deacetylase inhibitor and a medium chain fatty acid derivative as an absorption enhancer)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L42 ANSWER 3 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:356698 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 146:372833

TITLE: Histone deacetylase inhibitor or histone hyperacetylating agent for promoting wound healing and preventing scar formation

INVENTOR(S): Chung, Yih-Lin

PATENT ASSIGNEE(S): Taiwan

SOURCE: U.S. Pat. Appl. Publ., 36pp., Cont.-in-part of U.S. Ser. No. 205,738.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-----------------|
| US 20070072793 | A1 | 20070329 | US 2004-843025 | 20040510 <-- |
| US 20040018958 | A1 | 20040129 | US 2002-205738 | 20020725 <-- |
| US 6809118 | B2 | 20041026 | | |
| US 20060275370 | A1 | 20061207 | US 2006-499936 | 20060807 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-205738 | A2 20020725 <-- |
| | | | US 2004-798119 | A2 20040311 |
| | | | US 2004-843025 | A2 20040510 |

AB The invention discloses a method for promoting wound healing and preventing scar formation in a variety of wounds in skin, mucosa, and cornea. The method comprises administering a therapeutically effective amount of a histone deacetylase inhibitor or a hyperacetylating agent. The histone deacetylase inhibitor or hyperacetylating agent is capable of stimulating multiple cytokines/growth factors in the early phase of wound healing, and suppressing fibrogenic cytokines/growth factors in the late phase of tissue remodeling in the wound site, and is useful in promoting epithelial cell regrowth and reducing excessive collagen accumulation, which results in rapid wound closure with reduced scarring.

IT 9076-57-7, Histone deacetylase

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(histone deacetylase inhibitor or histone hyperacetylating agent for promoting wound healing and preventing scar formation, and use with other agents)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

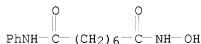
IT 149647-78-9, Suberoylanilide hydroxamic acid

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(histone deacetylase inhibitor or histone hyperacetylating agent for promoting wound healing and preventing scar formation, and use with other agents)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



L42 ANSWER 4 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1284568 CAPLUS <<LOGINID::20080505>>

DOCUMENT NUMBER: 146:50305

TITLE: Method and compositions for treatment of epithelial damage

INVENTOR(S): Chung, Yih-Lin; Pui, Nam-Mew

PATENT ASSIGNEE(S): Taiwan

SOURCE: U.S. Pat. Appl. Publ., 14pp., Cont.-in-part of U.S.

Ser. No. 843,025.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-----------------|
| US 20060275370 | A1 | 20061207 | US 2006-499936 | 20060807 <-- |
| US 20040018958 | A1 | 20040129 | US 2002-205738 | 20020725 <-- |
| US 6809118 | B2 | 20041026 | | |
| US 20050272644 | A1 | 20051208 | US 2004-798119 | 20040311 <-- |
| US 20070072793 | A1 | 20070329 | US 2004-843025 | 20040510 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-205738 | A2 20020725 <-- |
| | | | US 2004-798119 | A2 20040311 |
| | | | US 2004-843025 | A2 20040510 |

AB The present invention is directed to methods and compns. of treating or preventing epithelial lining tissue damage from dermatitis or mucositis induced by radiation exposure and/or chemotherapy, by applying to skin, mucosa or other tissues of the body an amount of a therapeutic composition

which

comprises a histone deacetylase inhibitor formulated with at least one pharmaceutically acceptable biocompatible polymer or carrier, or pharmaceutically acceptable salts in an amount sufficient to delay onset or decrease severity of the signs and symptoms of dermatitis and mucositis in cancer therapy. Such therapeutic compns. have the advantage of prolonged retention and sustained action of the histone deacetylase inhibitor in the skin, mucosa or other tissues of the body. The invention is also directed to treatment and prevention of gastrointestinal distress and cancer-related fatigue syndrome that are associated with mucositis in cancer therapy.

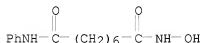
IT 9076-57-7

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitor; method and compns. for treatment of epithelial damage)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, Suberoylanilide hydroxamic acid
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (method and compns. for treatment of epithelial damage)
 RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



L42 ANSWER 5 OF 56 CAPLUS COPYRIGHT 2008 ACS ON STN
 ACCESSION NUMBER: 2005:1355554 CAPLUS <LOGINID:20080505>
 DOCUMENT NUMBER: 144:81158
 TITLE: Use of thioredoxin measurements for diagnostics and
 treatments
 INVENTOR(S): Marks, Paul A.; Ungerstedt, Johanna
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S.
 Ser. No. 369,094.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------------|
| US 20050288227 | A1 | 20051229 | US 2005-144301 | 20050603 <-- |
| US 20030235588 | A1 | 20031225 | US 2003-369094 | 20030214 <-- |
| US 20060009526 | A1 | 20060112 | US 2005-223405 | 20050909 <-- |
| US 20060009527 | A1 | 20060112 | US 2005-223547 | 20050909 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-357383P | P 20020215 <-- |
| | | | US 2003-369094 | A2 20030214 |
| | | | US 2004-577089P | P 20040604 |

AB The invention relates to methods for monitoring patient response to histone deacetylase inhibitors (e.g., suberoylanilide hydroxamic acid (SAHA)) or other therapeutic agents by measuring the level of thioredoxin in body fluids, tissues, and/or cells, such as peripheral blood mononuclear cells, plasma, or serum. The invention also relates to methods of monitoring and/or assisting with the diagnosis of a wide variety of thioredoxin-related diseases and conditions, such as inflammatory diseases, allergic diseases, autoimmune diseases, diseases associated with oxidative stress or diseases characterized by cellular hyperproliferation.

IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)

(use of thioredoxin expression measurements for diagnostics and monitoring treatments with histone deacetylase inhibitors and other therapeutic agents for hyperproliferative diseases)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

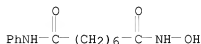
IT 149647-78-9, Suberoylanilide hydroxamic acid 382180-17-8
, Pyroxamide

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of thioredoxin expression measurements for diagnostics and monitoring treatments with histone deacetylase inhibitors and other therapeutic agents for hyperproliferative diseases)

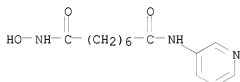
RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



RN 382180-17-8 CAPLUS

CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



L42 ANSWER 6 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1292833 CAPLUS <<LOGINID::20080505>>

DOCUMENT NUMBER: 144:32206

TITLE: Method using histone deacetylase inhibitors for increasing therapeutic gain in radiotherapy and chemotherapy

INVENTOR(S): Chung, Yih-Lin

PATENT ASSIGNEE(S): Taiwan

SOURCE: U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U.S. Ser. No. 205,738.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

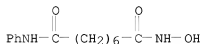
US 20050272644 A1 20051208 US 2004-798119 20040311 <--
US 20040018958 A1 20040129 US 2002-205738 20020725 <--
US 6809118 B2 20041026
US 20060275370 A1 20061207 US 2006-499936 20060807 <--
PRIORITY APPLN. INFO.: US 2002-205738 A2 20020725 <--
US 2004-798119 A2 20040311
US 2004-843025 A2 20040510

AB The invention provides compns. and methods for increasing therapeutic gain in radiotherapy and chemotherapy for proliferating malignant or nonmalignant disease to produce high probability of tumor control with low frequency of sequelae of therapy by administering a therapeutically effective amount of a histone deacetylase inhibitor. The compds. are capable of simultaneously stimulating epithelial regrowth, inhibiting fibroblast proliferation, decreasing collagen deposits, suppressing fibrogenic growth factor, subsiding proinflammatory cytokine, and modulating expression of cell cycle genes, tumor suppressors and oncogenes, and are useful for increasing the therapeutic gain in radiotherapy and chemotherapy, which results in decrease of skin swelling and inflammation, promotion of epithelial healing in mucosa and dermis, decrease of xerostomia, prevention/reduction of severity of plantar-palmar syndrome, prevention of tissue fibrosis, ulceration, necrosis and tumorigenesis, and increase of tumor growth inhibition and tumor therapy effectiveness.

IT 149647-78-9, Suberoylanilide hydroxamic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors for increasing therapeutic gain in radiotherapy and chemotherapy)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; histone deacetylase inhibitors for increasing therapeutic gain in radiotherapy and chemotherapy)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L42 ANSWER 7 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1103330 CAPLUS <LOGINID::20080505>
DOCUMENT NUMBER: 143:379844
TITLE: Methods using deacetylase inhibitors for treating neurodegenerative diseases and motor deficit disorders
INVENTOR(S): Steffan, Joan S.; Thompson, Leslie M.; Marsh, J. Lawrence; Bodai, Laszlo; Pallos, Judit; Hockly, Emma; Bates, Gillian
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 52 pp., Cont.-in-part of U.S. Ser. No. 476,627.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------------|
| US 20050227915 | A1 | 20051013 | US 2004-768292 | 20040129 <-- |
| WO 2002090534 | A1 | 20021114 | WO 2002-US14167 | 20020502 <-- |
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| | | | US 2001-288215P | P 20010502 <-- |
| | | | US 2002-372724P | P 20020411 <-- |
| | | | WO 2002-US14167 | W 20020502 <-- |
| | | | US 2003-443717P | P 20030129 |
| | | | US 2003-476627 | A2 20031030 |

OTHER SOURCE(S): MARPAT 143:379844

AB The invention discloses a method for treating a variety of diseases and disorders, including polyglutamine expansion diseases such as Huntington's disease, neurol. degeneration, psychiatric disorders, and protein aggregation disorders and diseases, comprising administering to patients in need thereof a therapeutically effective amount of one or more deacetylase inhibitors. The invention is also directed to a transgenic fly useful as a model of polyglutamine expansion diseases, which may be used to test potential therapeutic agents.

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (deacetylase inhibitors for treating neurodegenerative diseases and motor deficit disorders)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, Suberoylanilide hydroxamic acid 149647-78-9D

, Suberoylanilide hydroxamic acid, derivs. 382180-17-8,

Pyroxamide 382180-17-8D, Pyroxamide, derivs.

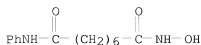
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(deacetylase inhibitors for treating neurodegenerative diseases and motor deficit disorders)

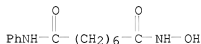
RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



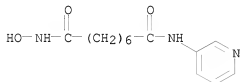
RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



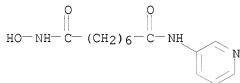
RN 382180-17-8 CAPLUS

CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



RN 382180-17-8 CAPLUS

CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



L42 ANSWER 8 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:177856 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 142:254579

TITLE: Method of treating cancer with histone deacetylase (HDAC) inhibitors

INVENTOR(S): Bacopoulos, Nicholas G.; Chiao, Judy H.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.

PATENT ASSIGNEE(S): Aton Pharma, Inc., USA; Sloan-Kettering Institute for Cancer Research

SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

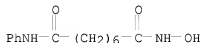
FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------------|
| WO 2005018578 | A2 | 20050303 | WO 2004-US27943 | 20040826 |
| WO 2005018578 | A3 | 20050512 | | |
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| US 20040087631 | A1 | 20040506 | US 2003-650025 | 20030826 <-- |
| US 7148257 | B2 | 20061212 | | |
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| AU 2004266169 | A1 | 20050303 | AU 2004-266169 | 20040826 |
| AU 2004266169 | A2 | 20060406 | | |
| AU 2004266169 | B2 | 20070503 | | |
| AU 2004266169 | B9 | 20070510 | | |
| CA 2535806 | A1 | 20050303 | CA 2004-2535806 | 20040826 |
| EP 1663194 | A2 | 20060607 | EP 2004-782425 | 20040826 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004013826 | A | 20061024 | BR 2004-13826 | 20040826 |
| CN 1870985 | A | 20061129 | CN 2004-80031306 | 20040826 |
| JP 2007518694 | T | 20070712 | JP 2006-524891 | 20040826 |
| KR 2007029617 | A | 20070314 | KR 2006-703748 | 20060224 |
| MX 2006PA02234 | A | 20060801 | MX 2006-PA2234 | 20060227 |
| NO 2006001348 | A | 20060523 | NO 2006-1348 | 20060324 |
| US 20070060614 | A1 | 20070315 | US 2006-567952 | 20061117 <-- |
| AU 2007203525 | A1 | 20070816 | AU 2007-203525 | 20070726 |
| AU 2007203648 | A1 | 20070823 | AU 2007-203648 | 20070803 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 2003-650025 | A1 20030826 |
| | | | US 2003-665079 | A1 20030916 |
| | | | US 2002-361759P | P 20020304 <-- |
| | | | AU 2003-213684 | A3 20030304 |
| | | | US 2003-379149 | A2 20030304 |
| | | | AU 2004-266169 | A3 20040826 |
| | | | WO 2004-US27943 | W 20040826 |

OTHER SOURCE(S): MARPAT 142:254579

AB The invention discloses methods for treating cancers, e.g. mesothelioma or lymphoma. More specifically, the invention discloses methods for treating mesothelioma or diffuse large B-cell lymphoma (DLBCL), by administration of pharmaceutical compns. comprising HDAC inhibitors, e.g., suberoylanilide hydroxamic acid (SAHA; preparation described). The oral formulations of the pharmaceutical compns. have favorable pharmacokinetic profiles such as high bioavailability and surprisingly give rise to high blood levels of the active compds. over an extended period of time. The invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a

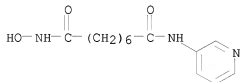
therapeutically effective amount of the HDAC inhibitors in vivo.
IT 149647-78-9P, Saha
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(histone deacetylase inhibitors for cancer treatment)
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(histone deacetylase inhibitors for cancer treatment)
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 382180-17-8, Pyroxamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors for cancer treatment)
RN 382180-17-8 CAPLUS
CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



L42 ANSWER 9 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:701812 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 141:167803
TITLE: Treatment of lung cells with histone deacetylase inhibitors
INVENTOR(S): Wiech, Norbert L.; Lan-Hargest, Hsuan-Yin
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp., Cont.-in-part of U.S. Ser. No. 25,947.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|------|----------|-----------------|--------------|
| US 20040167184 | A1 | 20040826 | US 2003-715377 | 20031119 <-- |
| US 7314953 | B2 | 20080101 | | |
| US 20020143196 | A1 | 20021003 | US 2001-812944 | 20010327 <-- |
| US 6495719 | B2 | 20021217 | | |
| US 20020143052 | A1 | 20021003 | US 2001-812945 | 20010327 <-- |
| US 7312247 | B2 | 20071225 | | |
| US 20020143037 | A1 | 20021003 | US 2001-25947 | 20011226 <-- |
| US 20030083521 | A1 | 20030501 | US 2002-307321 | 20021202 <-- |

PRIORITY APPLN. INFO.:

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|-----------------|----|--------------|
| US 2001-812940 | B1 | 20010327 <-- |
| US 2001-812944 | A3 | 20010327 <-- |
| US 2001-812945 | A2 | 20010327 <-- |
| US 2001-25947 | A2 | 20011226 <-- |
| US 2002-427567P | P | 20021120 <-- |
| US 2002-307321 | B2 | 20021202 <-- |

OTHER SOURCE(S): MARPAT 141:167803

AB Lung disease, such as cystic fibrosis, chronic obstructive pulmonary disease, asthma, or acute and chronic bronchitis, can be treated with an oxyamide-containing compound Preparation of e.g.

5-phenyl-2,4-pentadienoylhydroxamic acid is described.

IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (Treatment of lung cells with histone deacetylase inhibitors)

RN 9076-57-7 CAPLUS

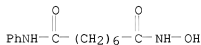
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, SAHA
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (Treatment of lung cells with histone deacetylase inhibitors)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



L42 ANSWER 10 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:550755 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 141:82311

TITLE: Methods of treating cancer with histone deacetylase (HDAC) inhibitors

INVENTOR(S): Bacopoulos, Nicholas G.; Chiao, Judy H.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M. USA

PATENT ASSIGNEE(S):

SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Pat. Appl. 2004 72,735.

CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------------|
| US 20040132825 | A1 | 20040708 | US 2003-692523 | 20031024 <-- |
| US 20040072735 | A1 | 20040415 | US 2003-379149 | 20030304 <-- |
| AU 2004283717 | A2 | 20050506 | AU 2004-283717 | 20041022 |
| AU 2004283717 | A1 | 20050506 | | |
| CA 2543319 | A1 | 20050506 | CA 2004-2543319 | 20041022 |
| WO 2005039498 | A2 | 20050506 | WO 2004-US35181 | 20041022 |
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| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1689379 | A2 | 20060816 | EP 2004-796215 | 20041022 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| CN 1901895 | A | 20070124 | CN 2004-80039156 | 20041022 |
| JP 2007509171 | T | 20070412 | JP 2006-536858 | 20041022 |
| IN 2006DN02367 | A | 20070803 | IN 2006-DN2367 | 20060428 |
| AU 2007203525 | A1 | 20070816 | AU 2007-203525 | 20070726 |
| AU 2007203648 | A1 | 20070823 | AU 2007-203648 | 20070803 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 2002-361759P | P 20020304 <-- |
| | | | US 2003-379149 | A2 20030304 |
| | | | AU 2003-213684 | A3 20030304 |
| | | | US 2003-692523 | A 20031024 |
| | | | AU 2004-266169 | A3 20040826 |
| | | | WO 2004-US35181 | W 20041022 |

OTHER SOURCE(S): MARPAT 141:82311

AB The invention discloses methods for treating cancers, e.g. leukemia. More specifically, the invention relates to methods of treating acute and chronic leukemias including Acute Lymphocytic Leukemia (ALL), Acute Myeloid Leukemia (AML), Chronic Lymphocytic leukemia (CLL), Chronic myeloid leukemia (CML) and Hairy Cell Leukemia, by administration of pharmaceutical compns. comprising HDAC inhibitors, e.g., suberoylanilide hydroxamic acid (SAHA; preparation described). The oral formulations of the pharmaceutical compns. have favorable pharmacokinetic profiles such as high bioavailability and surprisingly give rise to high blood levels of the active compds. over an extended period. The invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors *in vivo*.

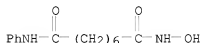
IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (histone deacetylase inhibitors for treatment of cancer)

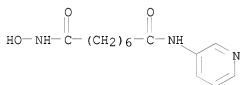
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9P, Suberoylanilide hydroxamic acid
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(histone deacetylase inhibitors for treatment of cancer)
RN 149647-78-9 CAPLUS
CN Octanediarnide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 382180-17-8, Pyroxarnide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors for treatment of cancer)
RN 382180-17-8 CAPLUS
CN Octanediarnide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



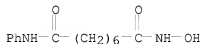
L42 ANSWER 11 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:533980 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 141:65091
TITLE: Methods of treating cancer with histone deacetylase (HDAC) inhibitors
INVENTOR(S): Bacopoulos, Nicholas G.; Chiao, Judy H.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 54 pp., Cont.-in-part of U.S. Ser. No. 379,149.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| US 20040127523 | A1 | 20040701 | US 2003-665079 | 20030916 <-- |

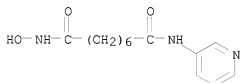
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 AU 2004266169 A1 20050303 AU 2004-266169 20040826
 AU 2004266169 A2 20060406
 AU 2004266169 B2 20070503
 AU 2004266169 B9 20070510
 CA 2535806 A1 20050303 CA 2004-2535806 20040826
 WO 2005018578 A2 20050303 WO 2004-US27943 20040826
 WO 2005018578 A3 20050512
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 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
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 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG
 EP 1663194 A2 20060607 EP 2004-782425 20040826
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 BR 2004013826 A 20061024 BR 2004-13826 20040826
 CN 1870985 A 20061129 CN 2004-80031306 20040826
 JP 2007518694 T 20070712 JP 2006-524891 20040826
 KR 2007029617 A 20070314 KR 2006-703748 20060224
 MX 2006PA02234 A 20060801 MX 2006-PA2234 20060227
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 US 20070060614 A1 20070315 US 2006-567952 20061117 <--
 AU 2007203525 A1 20070816 AU 2007-203525 20070726
 AU 2007203648 A1 20070823 AU 2007-203648 20070803
 PRIORITY APPLN. INFO.: US 2002-361759P P 20020304 <--
 US 2003-379149 A2 20030304
 AU 2003-213684 A3 20030304
 US 2003-650025 A 20030826
 US 2003-665079 A 20030916
 AU 2004-266169 A3 20040826
 WO 2004-US27943 W 20040826
 OTHER SOURCE(S): MARPAT 141:65091
 AB The invention relates to methods of treating cancers, e.g., lymphoma.
 More specifically, the present invention relates to methods of treating
 diffuse large B-cell lymphoma (DLBCL), by administration of pharmaceutical
 compns. comprising HDAC inhibitors, e.g., suberoylanilide hydroxamic acid
 (preparation described). The oral formulations of the pharmaceutical compns.
 have favorable pharmacokinetic profiles such as high bioavailability and
 surprisingly give rise to high blood levels of the active compns. over an
 extended period of time. The present invention further provides a safe,
 daily dosing regimen of these pharmaceutical compns., which is easy to
 follow, and which results in a therapeutically effective amount of the HDAC
 inhibitors in vivo.
 IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (histone deacetylase inhibitors for treatment of cancer)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9P, SAHA
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (histone deacetylase inhibitors for treatment of cancer)
 RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 382180-17-8, Pyroxamide
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (histone deacetylase inhibitors for treatment of cancer)
 RN 382180-17-8 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



L42 ANSWER 12 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:533979 CAPLUS <LOGINID:20080505>
 DOCUMENT NUMBER: 141:65090
 TITLE: Methods of treating cancer with histone deacetylase (HDAC) inhibitors
 INVENTOR(S): Chiao, Judy H.; Bacopoulos, Nicholas G.; Miller, Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 56 pp., Cont.-in-part of U.S. Ser. No. 379,149.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|------|----------|-----------------|--------------|
| US 20040127522 | A1 | 20040701 | US 2003-616649 | 20030709 <-- |
| US 20040072735 | A1 | 20040415 | US 2003-379149 | 20030304 <-- |
| AU 2007203525 | A1 | 20070816 | AU 2007-203525 | 20070726 |

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|------------------------|-------------|-----------------|----------------|
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| | | US 2003-379149 | A2 20030304 |
| | | AU 2003-213684 | A3 20030304 |
| | | AU 2004-266169 | A3 20040826 |

OTHER SOURCE(S): MARPAT 141:65090

AB The invention provides methods for treating cancers, chemoprevention, selectively inducing terminal differentiation, cell growth arrest and/or apoptosis of neoplastic cells, and/or inhibiting histone deacetylase (HDAC) by administration of pharmaceutical compns. comprising potent HDAC inhibitors. The oral bioavailability of the active compds. in the pharmaceutical compns. of the invention is surprisingly high. Moreover, the pharmaceutical compns. unexpectedly give rise to high, therapeutically effective blood levels of the active compds. over an extended period of time. The invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo. Compds. of the invention include e.g. suberoylanilide hydroxamic acid (preparation described).

IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (histone deacetylase inhibitors for treatment of cancer)

RN 9076-57-7 CAPLUS

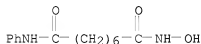
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9P, SAHA
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
 PREP (Preparation); USES (Uses)
 (histone deacetylase inhibitors for treatment of cancer)

RN 149647-78-9 CAPLUS

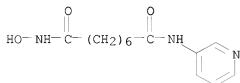
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 382180-17-8, Pyroxamide
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (histone deacetylase inhibitors for treatment of cancer)

RN 382180-17-8 CAPLUS

CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



L42 ANSWER 13 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:513346 CAPLUS <LOGINID:20080505>
 DOCUMENT NUMBER: 141:59733
 TITLE: Polymorphs of suberoylanilide hydroxamic acid, method of producing the same, and pharmaceutical composition containing the same
 INVENTOR(S): Miller, Thomas A.; Richon, Victoria M.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 60 pp., Cont.-in-part of U.S. Ser. No. 379,149.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------------|
| US 20040122101 | A1 | 20040624 | US 2003-600132 | 20030619 <-- |
| US 20040072735 | A1 | 20040415 | US 2003-379149 | 20030304 <-- |
| AU 2007203525 | A1 | 20070816 | AU 2007-203525 | 20070726 |
| AU 2007203648 | A1 | 20070823 | AU 2007-203648 | 20070803 |
| PRIORITY APPLN. INFO.: | | | US 2002-361759P | P 20020304 <-- |
| | | | US 2003-379149 | A2 20030304 |
| | | | AU 2003-213684 | A3 20030304 |
| | | | AU 2004-266169 | A3 20040826 |

AB The present invention provides methods of selectively inducing terminal differentiation, cell growth arrest and/or apoptosis of neoplastic cells, and/or inhibiting histone deacetylase (HDAC) by administration of pharmaceutical compns. comprising potent HDAC inhibitors. The oral bioavailability of the active compds. in the pharmaceutical compns. of the present invention is surprisingly high. Moreover, the pharmaceutical compns. unexpectedly give rise to high, therapeutically effective blood levels of the active compds. over an extended period of time. The present invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo. The present invention also provides a novel Form I polymorph of SAHA, characterized by a unique X-ray diffraction pattern and Differential Scanning Calorimetry profile, as well as a unique crystalline structure.

IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibition; polymorphs of suberoylanilide hydroxamic acid, method of producing the same, and pharmaceutical composition containing the same)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

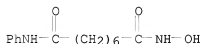
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9P, Suberoylanilide hydroxamic acid
 RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); PKT (Pharmacokinetics); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (polymorphs of suberoylanilide hydroxamic acid, method of producing the

same, and pharmaceutical composition containing the same)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



L42 ANSWER 14 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:485573 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 141:18132

TITLE: Induction of insulin expression by histone deacetylase inhibitors

INVENTOR(S): Levine, Fred; Itkin-Ansari, Pamela

PATENT ASSIGNEE(S): Regents of the University of California, USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

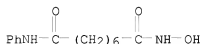
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-------------------------------|--------------|
| US 20040002447 | A1 | 20040101 | US 2002-162952 | 20020604 <-- |
| WO 2003103613 | A2 | 20031218 | WO 2003-US9986 | 20030401 <-- |
| WO 2003103613 | A3 | 20040401 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2003275026 | A1 | 20031222 | AU 2003-275026 | 20030401 <-- |
| EP 1509598 | A2 | 20050302 | EP 2003-757244 | 20030401 <-- |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| PRIORITY APPLN. INFO.: | | | US 2002-162952 A 20020604 <-- | |
| | | | WO 2003-US9986 W 20030401 | |
| AB | The present invention provides compns. and methods for inducing insulin expression in cells by contacting the cells with a histone deacetylase inhibitor. The methods comprise: providing a cell that expresses a PDX-1 or neuroD/BETA2 polynucleotide; and contacting the cell with a histone deacetylase inhibitor, thereby inducing insulin gene expression in the cells. The histone deacetylase inhibitors comprise butyrate, hydroxamic acids, cyclic peptides, benzamides, and GLP-1 receptor agonists. | | | |
| IT | 149647-78-9, Suberoyl anilide hydroxamic acid | | | |
| | RL: BUU (Biological use, unclassified); THU (Therapeutic use); | | | |

BIOL (Biological study); USES (Uses)
 (induction of insulin expression by histone deacetylase inhibitors)
 RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
 RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (inhibitors; induction of insulin expression by histone deacetylase
 inhibitors)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L42 ANSWER 15 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:450591 CAPLUS <<LOGINID:20080505>>
 DOCUMENT NUMBER: 141:17644
 TITLE: Use of a histone deacetylase inhibitor for the
 treatment of muscular dystrophies
 INVENTOR(S): De la Porte, Sabine; Israel, Maurice; Voisin, Vincent;
 Haddad, Hafedh
 PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique CNRS, Fr.
 SOURCE: Fr. Demande, 21 pp.
 CODEN: FRXXBL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| FR 2847817 | A1 | 20040604 | FR 2002-14980 | 20021128 <-- |
| FR 2847817 | B1 | 20061110 | | |
| CA 2507450 | A1 | 20040617 | CA 2003-2507450 | 20031128 <-- |
| WO 2004050076 | A1 | 20040617 | WO 2003-FR3530 | 20031128 <-- |
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| AU 2003294110 | A1 | 20040623 | AU 2003-294110 | 20031128 <-- |
| EP 1565175 | A1 | 20050824 | EP 2003-789530 | 20031128 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 US 20060148684 A1 20060706 US 2005-536417 20050927 <--
 PRIORITY APPLN. INFO.: FR 2002-14980 A 20021128 <--
 WO 2003-FR3530 W 20031128

AB The invention discloses the use of an inhibitor of histone deacetylase for the preparation of a drug intended for the treatment or the prevention of a disease resulting from the deficiency of an adult gene by the re-expression of homologous fetal gene. The invention is interested particularly in the treatment of dystrophies, e.g. Duchenne dystrophy or Becker's dystrophy, where the defective adult gene is the dystrophin gene and the homologous fetal gene is the utrophin gene.

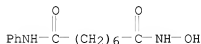
IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (histone deacetylase inhibitor for treatment of muscular dystrophies)

RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, Suberoylanilide hydroxamic acid
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (histone deacetylase inhibitor for treatment of muscular dystrophies)

RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 16 OF 56 CAPLUS COPYRIGHT 2008 ACS ON STN
 ACCESSION NUMBER: 2004:392325 CAPLUS <LOGINID::20080505>>
 DOCUMENT NUMBER: 140:386067
 TITLE: Histone deacetylase (HDAC) inhibitors for the treatment of ocular neovascular or edematous disorders and diseases
 INVENTOR(S): Klimko, Peter G.; Bingham, David P.
 PATENT ASSIGNEE(S): Alcon, Inc., Switz.
 SOURCE: U.S. Pat. Appl. Publ., 8 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|------|----------|-----------------|--------------|
| US 20040092558 | A1 | 20040513 | US 2003-697135 | 20031030 <-- |
| CA 2504460 | A1 | 20040527 | CA 2003-2504460 | 20031030 <-- |
| WO 2004043352 | A2 | 20040527 | WO 2003-US34617 | 20031030 <-- |
| WO 2004043352 | A3 | 20040715 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

AU 2003287349 A1 20040603 AU 2003-287349 20031030 <--
 EP 1560583 A2 20050810 EP 2003-781581 20031030 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003016206 A 20050927 BR 2003-16206 20031030 <--
 CN 1711087 A 20051221 CN 2003-80103003 20031030 <--
 JP 2006512318 T 20060413 JP 2004-551638 20031030 <--
 US 20060074100 A1 20060406 US 2005-531754 20050418 <--
 ZA 2005003237 A 20060628 ZA 2005-3237 20050421 <--
 IN 2005DN02544 A 20070202 IN 2005-DN2544 20050613 <--

PRIORITY APPLN. INFO.: US 2002-425574P P 20021112 <--
 WO 2003-US34617 W 20031030

OTHER SOURCE(S): MARPAT 140:386067

AB The invention discloses ophthalmic compns. containing HDAC inhibitors and their use for treating ocular neovascular or edematous diseases and disorders.

IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (histone deacetylase inhibitors for treatment of ocular neovascular or edematous diseases)

RN 9076-57-7 CAPLUS

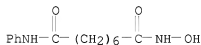
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9 329966-97-4 329967-02-4
 382180-17-8
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (histone deacetylase inhibitors for treatment of ocular neovascular or edematous diseases)

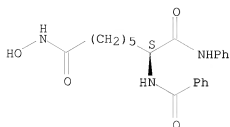
RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



RN 329966-97-4 CAPLUS
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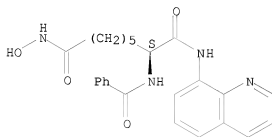
Absolute stereochemistry.



RN 329967-02-4 CAPLUS

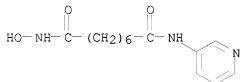
CN Octanediamide, 2-(benzoylamino)-N8-hydroxy-N1-8-quinolinyl-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 382180-17-8 CAPLUS

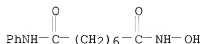
CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



L42 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:392299 CAPLUS <<LOGINID::20080505>>
 DOCUMENT NUMBER: 140:395534
 TITLE: Histone deacetylase inhibitors for treating degenerative diseases of the eye
 INVENTOR(S): Hellberg, Peggy E.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 5 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| US 20040092431 | A1 | 20040513 | US 2003-694309 | 20031027 <-- |
| CA 2504226 | A1 | 20040527 | CA 2003-2504226 | 20031027 <-- |
| WO 2004043348 | A2 | 20040527 | WO 2003-US33873 | 20031027 <-- |
| WO 2004043348 | A3 | 20040715 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR AU 2003286686 A1 20040603 AU 2003-286686 20031027 <-- EP 1562592 A2 20050817 EP 2003-777895 20031027 <-- R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK BR 2003016163 A 20050927 BR 2003-16163 20031027 <-- CN 1711086 A 20051221 CN 2003-80102935 20031027 <-- JP 2006508120 T 20060309 JP 2004-551572 20031027 <-- US 20070088045 A1 20070419 US 2005-531747 20050418 <-- ZA 2005003230 A 20060628 ZA 2005-3230 20050421 <-- MX 2005PA04738 A 20050803 MX 2005-PA4738 20050503 <-- US 20080004311 A1 20080103 US 2007-836309 20070809 <-- IN 2007DN07459 A 20071109 IN 2007-DN7459 20070927 <-- PRIORITY APPLN. INFO.: US 2002-425576P P 20021112 <-- US 2003-694309 A2 20031027 WO 2003-US33873 W 20031027 IN 2005-DN2543 A3 20050613 AB Comps. and methods for treating degenerative conditions and diseases of the eye with histone deacetylase inhibitors are disclosed. IT 149647-78-9, Suberoylanilide hydroxamic acid RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (histone deacetylase inhibitors for treating degenerative diseases of the eye) RN 149647-78-9 CAPLUS CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME) | | | | |



IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; histone deacetylase inhibitors for treating degenerative diseases of the eye)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L42 ANSWER 18 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:372881 CAPLUS <<LOGINID::20080505>>
 DOCUMENT NUMBER: 140:368663
 TITLE: Methods of treating cancer with hydroxamic acid
 derivative histone deacetylase (HDAC) inhibitors
 Bacopoulos, Nicholas G.; Chiao, Judy H.; Miller,
 Thomas A.; Paradise, Carolyn M.; Richon, Victoria M.
 USA
 INVENTOR(S):
 PATENT ASSIGNEE(S):
 SOURCE: U.S. Pat. Appl. Publ., 45 pp., Cont.-in-part of U.S.
 Ser. No. 3/9,149.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|----------------|
| US 20040087631 | A1 | 20040506 | US 2003-650025 | 20030826 <-- |
| US 7148257 | B2 | 20061212 | | |
| US 20040072735 | A1 | 20040415 | US 2003-379149 | 20030304 <-- |
| AU 2004266169 | A1 | 20050303 | AU 2004-266169 | 20040826 |
| AU 2004266169 | A2 | 20060406 | | |
| AU 2004266169 | B2 | 20070503 | | |
| AU 2004266169 | B9 | 20070510 | | |
| CA 2535806 | A1 | 20050303 | CA 2004-2535806 | 20040826 |
| WO 2005018578 | A2 | 20050303 | WO 2004-US27943 | 20040826 |
| WO 2005018578 | A3 | 20050512 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1663194 | A2 | 20060607 | EP 2004-782425 | 20040826 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| BR 2004013826 | A | 20061024 | BR 2004-13826 | 20040826 |
| CN 1870985 | A | 20061129 | CN 2004-80031306 | 20040826 |
| JP 2007518694 | T | 20070712 | JP 2006-524891 | 20040826 |
| KR 2007029617 | A | 20070314 | KR 2006-703748 | 20060224 |
| MX 2006PA022234 | A | 20060801 | MX 2006-PA2234 | 20060227 |
| NO 2006001348 | A | 20060523 | NO 2006-1348 | 20060324 |
| US 20060167103 | A1 | 20060727 | US 2006-391971 | 20060328 <-- |
| US 20070060614 | A1 | 20070315 | US 2006-567952 | 20061117 <-- |
| AU 2007203525 | A1 | 20070816 | AU 2007-203525 | 20070726 |
| AU 2007203648 | A1 | 20070823 | AU 2007-203648 | 20070803 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 2002-361759P | P 20020304 <-- |
| | | | US 2003-379149 | A2 20030304 |

| | |
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| AU 2003-213684 | A3 20030304 |
| US 2003-650025 | A 20030826 |
| US 2003-665079 | A 20030916 |
| AU 2004-266169 | A3 20040826 |
| WO 2004-US27943 | W 20040826 |

OTHER SOURCE(S): MARPAT 140:368663

AB The invention provides methods for treating cancers (e.g. mesothelioma), chemoprevention, selectively inducing terminal differentiation, cell growth arrest and/or apoptosis of neoplastic cells, and/or inhibiting histone deacetylase (HDAC) by administration of pharmaceutical compns. comprising potent HDAC inhibitors. The oral bioavailability of the active compds. in the pharmaceutical compns. of the invention is surprisingly high. Moreover, the pharmaceutical compns. unexpectedly give rise to high, therapeutically effective blood levels of the active compds. over an extended period of time. The invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo. HDAC inhibitors of the invention are hydroxamic acid derivs. e.g. suberoylanilide hydroxamic acid (SAHA; preparation described).

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (hydroxamic acid derivative histone deacetylase inhibitors for treatment of cancer)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

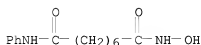
IT 149647-78-9P, Suberoylanilide hydroxamic acid

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hydroxamic acid derivative histone deacetylase inhibitors for treatment of cancer)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



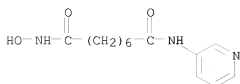
IT 382180-17-8, Pyroxamide

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hydroxamic acid derivative histone deacetylase inhibitors for treatment of cancer)

RN 382180-17-8 CAPLUS

CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)

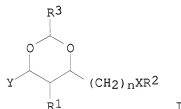


REFERENCE COUNT: 185 THERE ARE 185 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 19 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:310834 CAPLUS <<LOGINID:20080505>>
 DOCUMENT NUMBER: 140:339332
 TITLE: Preparation of trisubstituted dioxanes as histone deacetylase inhibitors.
 INVENTOR(S): Schreiber, Stuart L.; Sternson, Scott M.; Wong, Jason C.; Grozinger, Christina M.; Haggarty, Stephen J.; Koeller, Kathryn M.
 PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
 SOURCE: U.S. Pat. Appl. Publ., 177 pp., Cont.-in-part of U.S. Pat. Appl. 2003 187,027.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-----------------|
| US 20040072849 | A1 | 20040415 | US 2003-621276 | 20030717 <-- |
| US 7244853 | B2 | 20070717 | | |
| US 20030187027 | A1 | 20031002 | US 2002-144316 | 20020509 <-- |
| PRIORITY APPLN. INFO.: | | | US 2001-289850P | P 20010509 <-- |
| | | | US 2002-144316 | A2 20020509 <-- |

OTHER SOURCE(S): MARPAT 140:339332
 GI



AB Title compds. [I; R1, Y = H, aliphaticyl, alicyclyl, heteroaliphaticyl, heterocyclyl, aryl, heteroaryl; n = 1-5; R2 = R1, protecting group; X = O, S, C(R2a)2, NR2a; R2R2a = atoms to form alicyclyl, heterocyclyl, aryl,

heteroaryl; R3 = alipharyl, alicyclyl, heteroalipharyl, heterocyclyl, aryl, heteroaryl, were claimed. Thus, rel-N-[4-[(2R,4R,6S)-4-[[4,5-diphenyl-2-oxazolyl]thio]methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-octanediamide (tubacin, claimed compound) at ≥ 125 nM in A549 cells strongly increased α -tubulin acetylation levels. The present invention addnl. provides methods for modulating the glucose-sensitive subset of genes downstream of Ure2p.

IT 537049-40-4P, Tubacin

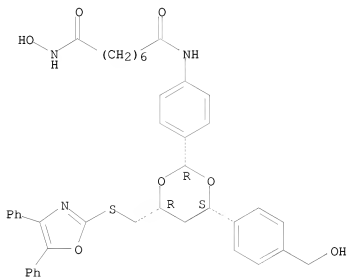
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

RN 537049-40-4 CAPLUS

CN Octanediamide, N1-[4-[(2R,4R,6S)-4-[[4,5-diphenyl-2-oxazolyl]thio]methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N8-hydroxy-, rel- (CA INDEX NAME)

Relative stereochemistry.



IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors, HDAC1 or HDAC6; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 438496-81-2, Tubulin deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

RN 438496-81-2 CAPLUS

CN Deacetylase, nicotinamide adenine dinucleotide-dependent protein (CA INDEX NAME)

INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 394657-69-3P

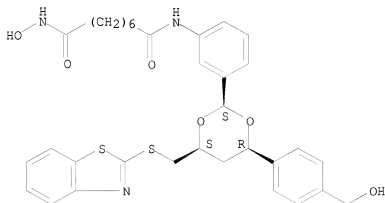
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of trisubstituted dioxanes as histone deacetylase inhibitors)

RN 394657-69-3 CAPLUS

CN Octanediamide, N-[3-[(2R,4R,6S)-4-[(2-benzothiazolylthio)methyl]-6-[4-(hydroxymethyl)phenyl]-1,3-dioxan-2-yl]phenyl]-N'-hydroxy-, rel- (9CI)
(CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 20 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:269998 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 140:247047

TITLE:

Method of treating leukemia with a combination of
suberoylanilide hydroxamic acid and imatinib mesylate
Bhalla, Kapil N.; Nimmanapalli, Ramedevi

INVENTOR(S):
PATENT ASSIGNEE(S): University of South Florida, USA

SOURCE: PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|--------------|
| WO 2004026234 | A2 | 20040401 | WO 2003-US28964 | 20030919 <-- |
| WO 2004026234 | A3 | 20040708 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
 TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2499189 A1 20040401 CA 2003-2499189 20030919 <--
 AU 2003270668 A1 20040408 AU 2003-270668 20030919 <--
 US 20040127571 A1 20040701 US 2003-605283 20030919 <--
 EP 1545536 A2 20050629 EP 2003-752375 20030919 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: US 2002-319563P P 20020919 <--
 US 2003-605283 A 20030919
 WO 2003-US28964 W 20030919

AB The invention discloses a method for inducing apoptosis, or increasing the rate or extent of apoptosis, in target cells. The method comprises contacting the cancer cells with an apoptosis-inducing amount of a tyrosine kinase inhibitor, imatinib mesylate, and a histone deacetylase inhibitor, suberoylanilide Hydroxamic Acid (SAHA). The method is applicable to ameliorating the resistance of the accelerated and blast phases of CML (CML-BC) to imatinib mesylate.

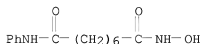
IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; suberoylanilide hydroxamic acid-imatinib mesylate combination for leukemia treatment)

RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, Suberoylanilide hydroxamic acid
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (suberoylanilide hydroxamic acid-imatinib mesylate combination for leukemia treatment)

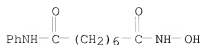
RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



L42 ANSWER 21 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:252351 CAPLUS <<LOGINID::20080505>>
 DOCUMENT NUMBER: 140:264488
 TITLE: Combination of a benzamide derivative and a histone deacetylase inhibitor for the treatment of leukemia
 INVENTOR(S): Dent, Paul; Grant, Steven; Krystal, Geoffrey; Yu, Chunrong
 PATENT ASSIGNEE(S): Virginia Commonwealth University, USA; Mcguire Va Medical Center 111k

SOURCE: PCT Int. Appl., 37 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|----------------|
| WO 2004024160 | A1 | 20040325 | WO 2003-IB4053 | 20030910 <-- |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW | | | |
| RW: | AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR | | | |
| CA 2498210 | A1 | 20040325 | CA 2003-2498210 | 20030910 <-- |
| AU 2003259521 | A1 | 20040430 | AU 2003-259521 | 20030910 <-- |
| BR 2003014112 | A | 20050712 | BR 2003-14112 | 20030910 <-- |
| EP 1553948 | A1 | 20050720 | EP 2003-795175 | 20030910 <-- |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| CN 1681505 | A | 20051012 | CN 2003-821763 | 20030910 <-- |
| JP 2006501267 | T | 20060112 | JP 2004-535791 | 20030910 <-- |
| US 20060100140 | A1 | 20060511 | US 2005-527553 | 20050909 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-410286P | P 20020913 <-- |
| | | | US 2002-411344P | P 20020918 <-- |
| | | | WO 2003-IB4053 | W 20030910 |
| AB | The invention pertains to a combination of a histone deacetylase inhibitor and N-[5-[4-(4-methyl-piperazino-methyl)-benzoylamido]-2-methylphenyl]-4-(3-pyridyl)-2-pyrimidine (I) or a pharmaceutically acceptable salt thereof for simultaneous, sep. or sequential use for the treatment of leukemia and especially Compound I-resistant leukemia. The histone deacetylase inhibitor is selected from sodium butyrate, MS 275, SAHA, aphacidin, depsi peptide, FK 228, trichostatin A, etc. For example, exposure of K562 cells for 24 h to Compound I concns. as high as 300 nM negligibly induced apoptosis, while 2.0 μM SAHA administered alone was also minimally toxic. However, when cells were exposed to SAHA in combination with 100 nM Compound I, a clear increase in apoptosis was observed (i.e., .apprx.20%), and for Compound I concentration of 250 nM, the large majority of cells (i.e., .apprx.75%) were apoptotic. Median Dose Effect anal. of apoptosis induction over a range of Compound I and SAHA concns. yielded Combination Index (CI) values lower than 1.0, corresponding to a synergistic interaction. | | | |
| IT | 149647-78-9, SAHA RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combination of histone deacetylase inhibitor and antitumor benzamide derivative for treatment of leukemia) | | | |
| RN | 149647-78-9 CAPLUS | | | |
| CN | Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME) | | | |



IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; combination of histone deacetylase inhibitor and antitumor
 benzamide derivative for treatment of leukemia)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 22 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:182726 CAPLUS <<LOGINID::20080505>>
 DOCUMENT NUMBER: 140:229435
 TITLE: Arthrodial cartilage extracellular matrix degradation
 inhibitor
 INVENTOR(S): Yamaji, Noboru; Shindou, Nobuaki; Terada, Yoh
 PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| WO 2004017996 | A1 | 20040304 | WO 2003-JP10460 | 20030819 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2495354 | A1 | 20040304 | CA 2003-2495354 | 20030819 <-- |
| AU 2003254951 | A1 | 20040311 | AU 2003-254951 | 20030819 <-- |
| EP 1547617 | A1 | 20050629 | EP 2003-792716 | 20030819 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 20050272647 | A1 | 20051208 | US 2005-525015 | 20050217 <-- |
| PRIORITY APPLN. INFO.: | | | JP 2002-239203 | A 20020820 <-- |
| | | | WO 2003-JP10460 | W 20030819 |

AB An arthrodial cartilage extracellular matrix degradation inhibitor, which contains a compound inhibiting histone deacetylase as the active ingredient, is useful in preventing and treating diseases and pathol. conditions in which the degradation and denaturation of arthrodial cartilage extracellular

matrix participate, in particular, osteoarthritis, articular rheumatism, arthritis deformans, etc.

IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (arthrodial cartilage extracellular matrix degradation inhibitor)

RN 9076-57-7 CAPLUS

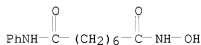
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, SAHA
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (arthrodial cartilage extracellular matrix degradation inhibitor)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

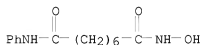
L42 ANSWER 23 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:117798 CAPLUS <LOGINID:20080505>>
 DOCUMENT NUMBER: 140:139491
 TITLE: BCR-ABL tyrosine kinase and histone deacetylase inhibitors as antitumor agents for treatment of chronic myelocytic leukemia and PH-pos. acute lymphoid leukemia
 INVENTOR(S): Karato, Masayuki
 PATENT ASSIGNEE(S): Nagoya Industrial Science Research Institute, Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|---|------|----------|-----------------|--------------|
| | JP 2004043390 | A | 20040212 | JP 2002-204889 | 20020712 <-- |
| PRIORITY APPLN. INFO.: | | | | JP 2002-204889 | 20020712 <-- |
| AB | BCR-ABL tyrosine kinase inhibitors, including imatinib mesylate, and histone deacetylase inhibitors, e.g. valproic acid, phenylbutyrate, SAHA, FR901228, MS 27275, and CHAPs, are claimed as antitumor agents for treatment of chronic myelocytic leukemia and PH-pos. acute lymphoid leukemia. The two enzyme inhibitors had synergistic antitumor actions with each others. | | | | |
| IT | 9076-57-7, Histone deacetylase RL: BSU (Biological study, unclassified); BIOL (Biological study) (BCR-ABL tyrosine kinase and histone deacetylase inhibitors as antitumor agents for treatment of chronic myelocytic leukemia and | | | | |

PH-pos. acute lymphoid leukemia)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, SAHA
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (BCR-ABL tyrosine kinase and histone deacetylase inhibitors as
 antitumor agents for treatment of chronic myelocytic leukemia and
 PH-pos. acute lymphoid leukemia)
 RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



L42 ANSWER 24 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:80835 CAPLUS <<LOGINID::20080505>>
 DOCUMENT NUMBER: 140:151933
 TITLE: Stents capable of controllably releasing histone
 deacetylase inhibitors
 INVENTOR(S): Tseng, Xufan; Xu, Shuyun
 PATENT ASSIGNEE(S): Advanced Stent Technologies, Inc., USA
 SOURCE: PCT Int. Appl., '73 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

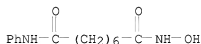
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|---|----------------|
| WO 2004009771 | A2 | 20040129 | WO 2003-US22449 | 20030718 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003249309 | A1 | 20040209 | AU 2003-249309 | 20030718 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-397780P | P 20020724 <-- |
| | | | US 2002-402086P | P 20020809 <-- |
| | | | WO 2003-US22449 | W 20030718 |
| AB | | | A stent device includes a stent body and one or more HDAC inhibitor depot(s) provided on or in the stent body, the depot(s) capable of controllably releasing HDAC inhibitor(s). Methods of using the stents in | |

treating and/or preventing restenosis are provided. A delivery system including the stent device and a methods of using the delivery system in treating and/or preventing restenosis are also provided. Kits comprising stents are provided. Trichostatin A inhibited human aortic SMC proliferation in vitro in a dose-dependent manner.

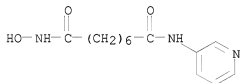
IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stents capable of controllably releasing histone deacetylase inhibitors)
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, SAHA 382180-17-8, Pyroxamide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stents capable of controllably releasing histone deacetylase inhibitors)
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



RN 382180-17-8 CAPLUS
CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



L42 ANSWER 25 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:855790 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 139:345907
TITLE: Combination therapy for the treatment of cancer using histone deacetylase inhibitors and radiotherapy
INVENTOR(S): Sgouros, George; Richon, Victoria M.; Marks, Paul A.; Rifkind, Richard A.
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| WO 2003088954 | A1 | 20031030 | WO 2003-US11812 | 20030415 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2482508 | A1 | 20031030 | CA 2003-2482508 | 20030415 <-- |
| AU 2003226408 | A1 | 20031103 | AU 2003-226408 | 20030415 <-- |
| AU 2003226408 | B2 | 20070614 | | |
| US 20040018968 | A1 | 20040129 | US 2003-413422 | 20030415 <-- |
| EP 1501489 | A1 | 20050202 | EP 2003-747011 | 20030415 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003009280 | A | 20050222 | BR 2003-9280 | 20030415 <-- |
| JP 2005530734 | T | 20051013 | JP 2003-585706 | 20030415 <-- |
| CN 1728991 | A | 20060201 | CN 2003-813849 | 20030415 <-- |
| MX 2004PA10199 | A | 20050705 | MX 2004-PA10199 | 20041015 <-- |
| IN 2006DN07048 | A | 20070713 | IN 2006-DN7048 | 20061123 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-373033P | P 20020415 <-- |
| | | | WO 2003-US11812 | W 20030415 |
| | | | IN 2004-DN3312 | A3 20041026 |

OTHER SOURCE(S): MARPAT 139:345907

AB The present invention relates to a method for the treatment of cancer in a patient in need thereof. The method comprises administering to a patient in need thereof a first amount of a histone deacetylase inhibitor in a first treatment procedure, and a second amount or dose of radiation in a second treatment procedure. The first and second treatments together comprise a therapeutically effective amount. The combination of the HDAC inhibitor and radiation therapy is therapeutically synergistic.

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combination therapy for treatment of cancer using histone deacetylase inhibitors and radiotherapy)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

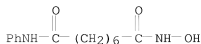
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, SAHA 382180-17-8, Pyroxamide

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for treatment of cancer using histone deacetylase inhibitors and radiotherapy)

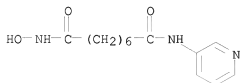
RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



RN 382180-17-8 CAPLUS

CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 26 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:796863 CAPLUS <<LOGINIP:20080505>>

DOCUMENT NUMBER: 139:286376

TITLE: Histone deacetylase inhibitors for the treatment of multiple sclerosis, amyotrophic lateral sclerosis and Alzheimer's disease

INVENTOR(S): Dangond, Fernando

PATENT ASSIGNEE(S): Brigham and Women's Hospital, Inc., USA

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

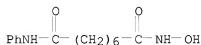
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|----------------|
| WO 2003083067 | A2 | 20031009 | WO 2003-US9273 | 20030327 <-- |
| WO 2003083067 | A8 | 20040819 | | |
| WO 2003083067 | A3 | 20050324 | | |
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| AU 2003226014 | A1 | 20031013 | AU 2003-226014 | 20030327 <-- |
| US 20040077591 | A1 | 20040422 | US 2003-401274 | 20030327 <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-368228P | P 20020328 <-- |
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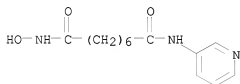
AB The present invention provide therapies for Alzheimer's disease (AD), multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS). The method relies on the use of an HDAC inhibitor, alone or in combination with other drugs, to prevent or treat AD, MS or ALS. Also provided are

methods of screening for addnl. HDAC inhibitors with particular efficacy against these disease states. Modulation of expression of genes, involved in neuroprotection and immune regulation, by HDAC inhibitors were demonstrated.

IT 149647-78-9, Suberoylanilide hydroxamic acid 382180-17-8
Pyroxamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HDAC inhibitor; histone deacetylase inhibitors for treatment of multiple sclerosis, amyotrophic lateral sclerosis and Alzheimer's disease)
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



RN 382180-17-8 CAPLUS
CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; histone deacetylase inhibitors for treatment of multiple sclerosis, amyotrophic lateral sclerosis and Alzheimer's disease)
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L42 ANSWER 27 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:737519 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 139:240347
TITLE: Methods of inducing terminal differentiation
INVENTOR(S): Richon, Victoria M.
PATENT ASSIGNEE(S): Aton Pharma, Inc., USA
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2003075839 | A2 | 20030918 | WO 2003-US6451 | 20030304 <-- |
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| AU 2003213684 | A1 | 20030922 | AU 2003-213684 | 20030304 <-- |
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| EP 1487426 | A2 | 20041222 | EP 2003-711372 | 20030304 <-- |
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| CN 1720034 | A | 20060111 | CN 2003-809589 | 20030304 <-- |
| RU 2320331 | C2 | 20080327 | RU 2004-133675 | 20030304 <-- |
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| AU 2007203525 | A1 | 20070816 | AU 2007-203525 | 20070726 |
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| | | | AU 2003-213684 | A3 20030304 |
| | | | WO 2003-US6451 | W 20030304 |
| | | | AU 2004-266169 | A3 20040826 |
| | | | KR 2004-713883 | A3 20040904 |
| | | | IN 2004-DN2721 | A3 20040915 |

OTHER SOURCE(S): MARPAT 139:240347

AB The present invention provides methods of selectively inducing terminal differentiation, cell growth arrest and/or apoptosis of neoplastic cells, and/or inhibiting histone deacetylase (HDAC) by administration of pharmaceutical compns. comprising potent HDAC inhibitors. The oral bioavailability of the active compds. such as such as suberoylanilide hydroxamic acid (SAHA) in the pharmaceutical compns. of the present invention is surprisingly high. Moreover, the pharmaceutical compns. unexpectedly give rise to high, therapeutically effective blood levels of the active compds. over an extended period of time. The present invention further provides a safe, daily dosing regimen of these pharmaceutical compns., which is easy to follow, and which results in a therapeutically effective amount of the HDAC inhibitors in vivo.

IT 9076-57-7, Histone deacetylase

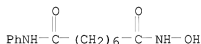
RL: BSU (Biological study, unclassified); BIOL (Biological study) (methods of inducing terminal differentiation of neoplastic cells using histone deacetylase inhibitors such as suberoylanilide hydroxamic acid with good bioavailability)

RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

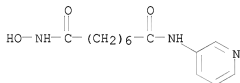
IT 149647-78-9P, Suberoylanilide hydroxamic acid
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)
(methods of inducing terminal differentiation of neoplastic cells using histone deacetylase inhibitors such as suberoylanilide hydroxamic acid with good bioavailability)

RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 382180-17-8, Pyroxamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of inducing terminal differentiation of neoplastic cells using histone deacetylase inhibitors such as suberoylanilide hydroxamic acid with good bioavailability)

RN 382180-17-8 CAPLUS
CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



L42 ANSWER 28 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:473272 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 139:47148
TITLE: Method of treating autoimmune diseases
INVENTOR(S): Kammer, Gary M.; Mishra, Nilamadhab
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S. Ser. No. 718,195.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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US 20030114525      A1      20030619      US 2002-151481      20020520 <--
US 7271198          B2      20070918
WO 2002055017      A2      20020718      WO 2001-US43871      20011119 <--
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    PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
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    BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 20060030626      A1      20060209      US 2005-237245      20050928 <--
US 20060178437      A1      20060810      US 2006-403608      20060413 <--
US 2000-718195      B2      20001120 <--
WO 2001-US43871      A      20011119 <--
US 2002-151481      A3      20020520 <--
US 2002-187586      A3      20020702 <--

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PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 139:47148

AB A method of treating an autoimmune disease comprising administering to the subject a treatment effective amount of a histone hyperacetylating agent, or a pharmaceutically acceptable salt thereof.

IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitor; method of treating autoimmune diseases using a histone hyperacetylating agent)

RN 9076-57-7 CAPLUS

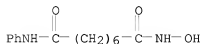
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, Suberoylanilide Hydroxamic acid
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (method of treating autoimmune diseases using a histone hyperacetylating agent)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)

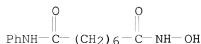


REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 29 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:335262 CAPLUS <LOGINID:20080505>
 DOCUMENT NUMBER: 138:349698
 TITLE: Screening system for modulators of gene HER2
 (neu/ErbB2) transcription, HER2 modulators identified thereby, and methods involving HER2 SNPs

INVENTOR(S): Benz, Christopher C.
 PATENT ASSIGNEE(S): Buck Institute for Age Research, USA
 SOURCE: PCT Int. Appl., 103 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|----------------|
| WO 2003035843 | A2 | 20030501 | WO 2002-US34288 | 20021025 <-- |
| WO 2003035843 | A3 | 20040826 | | |
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| AU 2002353891 | A1 | 20030506 | AU 2002-353891 | 20021025 <-- |
| US 20050123896 | A1 | 20050609 | US 2004-493141 | 20041025 <-- |
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| | | | US 2001-335290P | P 20011130 <-- |
| | | | US 2002-374161P | P 20020417 <-- |
| | | | WO 2002-US34288 | W 20021025 <-- |
| AB | This invention pertains to the development of a screening system to identify (screen for) gene HER2 (neu/ErbB2) promoter silencing agents. Such agents are expected to be of therapeutic value in the treatment of cancers characterized by HER2 amplification/upregulation. In addition, this invention pertains to the discovery that histone deacetylase (HDAC) inhibitors like sodium butyrate and trichostatin A (TSA), in a time and dose dependent fashion can silence genomically integrated and/or amplified/overexpressing promoters, such as that driving the HER2 (neu/ErbB2) oncogene, resulting in inhibition of gene products including transcripts and protein, and subsequent production of tumor/cell growth inhibition, apoptosis and/or differentiation. In another embodiment, this invention provides novel single nucleotide polymorphisms (SNPs) associated with the coding region of the HER2 proto-oncogene. The SNPs are indicators for altered risk, for developing ErbB2-pos. cancer in a mammal. | | | |
| IT | 149647-78-9, SAHA RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (histone deacetylase inhibitor; screening system for modulators of gene HER2 (neu/ErbB2) transcription and HER2 modulators identified thereby) | | | |
| RN | 149647-78-9 CAPLUS | | | |
| CN | Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME) | | | |



IT 9076-57-7, Histone deacetylase
 RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (inhibitor; screening system for modulators of gene HER2 (neu/ErbB2)
 transcription and HER2 modulators identified thereby)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L42 ANSWER 30 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:319660 CAPLUS <<LOGINID::20080505>>
 DOCUMENT NUMBER: 138:314634
 TITLE: Use of a histone deacetylase (HDAC) inhibitor for the
 treatment of neurodegenerative diseases and cancer of
 the brain
 INVENTOR(S): Richon, Victoria M.; Marks, Paul A.; Rifkind, Richard
 A.
 PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA
 SOURCE: PCT Int. Appl., 88 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|-----------------|
| WO 2003032921 | A2 | 20030424 | WO 2002-US33246 | 20021016 <-- |
| WO 2003032921 | A3 | 20031030 | | |
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| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
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| AU 2002340253 | A1 | 20030428 | AU 2002-340253 | 20021016 <-- |
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| | | | WO 2002-US33246 | W 20021016 <-- |

OTHER SOURCE(S): MARPAT 138:314634
 AB A method is provided for inhibiting HDAC in the brain of a mammal. The

method comprises administering to a mammal a HDAC inhibiting amount of a histone deacetylase inhibitor compound. Also provided is a method for treating diseases of the central nervous system (CNS) comprising administering a therapeutically effective amount of an inhibitor of HDAC. In particular embodiments, the CNS disease is a neurodegenerative disease. In further embodiments, the neurodegenerative disease is an inherited neurodegenerative disease, such as those inherited neurodegenerative diseases which are polyglutamine expansion diseases. In other embodiments, the disorder is cancer of the brain. The individual is a mammal, e.g. a primate or human.

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (histone deacetylase inhibitor for treatment of neurodegenerative diseases and brain cancer)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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329966-97-4 329966-98-5 329967-00-2

329967-01-3 329967-02-4 382180-17-8

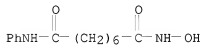
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RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(histone deacetylase inhibitor for treatment of neurodegenerative diseases and brain cancer)

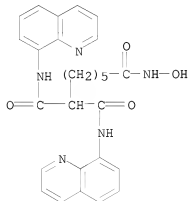
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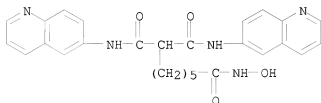
RN 329966-68-9 CAPLUS

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RN 329966-92-9 CAPLUS

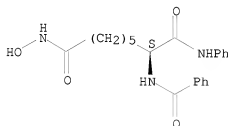
CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-di-6-quinolinyl- (9CI) (CA INDEX NAME)



RN 329966-97-4 CAPLUS

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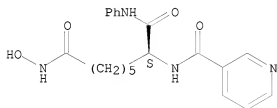
Absolute stereochemistry.



RN 329966-98-5 CAPLUS

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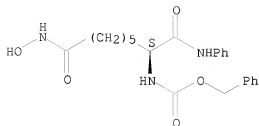
Absolute stereochemistry.



RN 329967-00-2 CAPLUS

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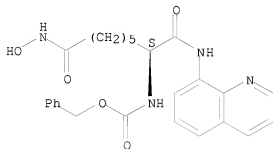
Absolute stereochemistry.



RN 329967-01-3 CAPLUS

CN Carbamic acid, N-[(1S)-7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, phenylmethyl ester (CA INDEX NAME)

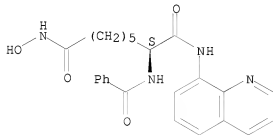
Absolute stereochemistry.



RN 329967-02-4 CAPLUS

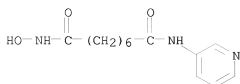
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Absolute stereochemistry.

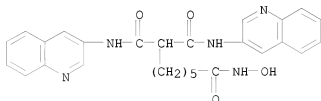


RN 382180-17-8 CAPLUS

CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



RN 512170-05-7 CAPLUS
 CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-di-3-quinolinyl- (9CI) (CA
 INDEX NAME)



L42 ANSWER 31 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:259705 CAPLUS <LOGINID:20080505>
 DOCUMENT NUMBER: 138:292737
 TITLE: Inhibition of histone deacetylase as a treatment for
 cardiac hypertrophy
 INVENTOR(S): Bristow, Michael R.; Long, Carlin; McKinsey, Timothy
 A.; Olson, Eric N.
 PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA;
 The Regents of the University of Colorado
 SOURCE: Eur. Pat. Appl., 39 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

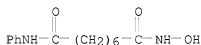
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| EP 1297851 | A1 | 20030402 | EP 2002-21676 | 20020927 <-- |
| EP 1297851 | B1 | 20050126 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| US 20030144340 | A1 | 20030731 | US 2002-256221 | 20020926 <-- |
| US 6706686 | B2 | 20040316 | | |
| JP 2003238445 | A | 20030827 | JP 2002-284313 | 20020927 <-- |
| AT 287731 | T | 20050215 | AT 2002-21676 | 20020927 <-- |
| PT 1297851 | T | 20050630 | PT 2002-21676 | 20020927 <-- |
| ES 2236415 | T3 | 20050716 | ES 2002-21676 | 20020927 <-- |
| EP 1605262 | A1 | 20051214 | EP 2005-1443 | 20020927 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK | | | | |

US 20040186049 A1 20040923 US 2004-801985 20040316 <--
 US 6946441 B2 20050920
 US 20060025333 A1 20060202 US 2005-190074 20050726 <--
 US 20060069014 A1 20060330 US 2005-215844 20050830 <--
 PRIORITY APPLN. INFO.: US 2001-325311P P 20010927 <--
 US 2001-334041P P 20011031 <--
 US 2002-256221 A1 20020926 <--
 EP 2002-21676 A3 20020927 <--
 US 2004-801985 A1 20040316
 US 2005-190074 A1 20050726

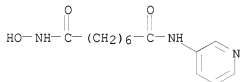
AB The present invention provides for methods of treating and preventing cardiac hypertrophy. Class II HDACs, which are known to participate in regulation of chromatin structure and gene expression, have been shown to have beneficial effects on cardiac hypertrophy. Surprisingly, the present invention demonstrates that HDAC inhibitors inhibit cardiac hypertrophy by inhibiting fetal cardiac gene expression and interfering with sarcomeric organization. Inhibitors include trichostatin A, trapoxin B, MS 275-27, m-carboxycinnamic acid bis-hydroxamide, depudecin, oxamflatin, apicidin, suberoylanilide hydroxamic acid, Scriptaid, etc.

IT 149647-78-9, Suberoylanilide hydroxamic acid 382180-17-8
 , Pyroxamide
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inhibition of histone deacetylase as a treatment for cardiac hypertrophy)

RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



RN 382180-17-8 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



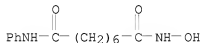
IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; inhibition of histone deacetylase as a treatment for cardiac hypertrophy)

RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 32 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:72949 CAPLUS <<LOGINID::20080505>>
DOCUMENT NUMBER: 139:190760
TITLE: Histone deacetylase inhibitors potently repress CXCR4 chemokine receptor expression and function in acute lymphoblastic leukemia
AUTHOR(S): Crazzolara, Roman; Johrer, Karin; Johnstone, Ricky W.; Greil, Richard; Kofler, Reinhard; Meister, Bernhard; Bernhard, David
CORPORATE SOURCE: Tyrolean Cancer Research Institute, Tyrolean Cancer Research Institute, University of Innsbruck, Innsbruck, Austria
SOURCE: British Journal of Haematology (2002), 119(4), 965-969
CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The chemokine receptor CXCR4 plays a crucial role in the survival and trafficking of leukemia cells and requires further attention as human immunodeficiency virus type I (HIV-1) utilizes CXCR4 as the major coreceptor for cellular entry. We demonstrated that inhibitors of histone deacetylases, currently being tested in clin. trials for the treatment of various tumors, extensively downregulated CXCR4 protein and mRNA levels in leukemia cell lines and lymphoblasts from patients with childhood acute leukemia. As a result, the ability of stromal cell-derived factor-1 to induce cellular migration was impaired. Repression of CXCR4 transcription by inhibitors of histone deacetylases might therefore represent a promising novel approach in the treatment of acute leukemias.
IT 149647-78-9, Suberoylanilide hydroxamic acid
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors repression of CXCR4 chemokine receptor in ALL)
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



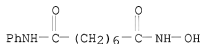
IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; histone deacetylase inhibitors repression of CXCR4 chemokine receptor in ALL)
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 33 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2003:52271 CAPLUS <<LOGINID::20080505>>
 DOCUMENT NUMBER: 139:172905
 TITLE: Histone acetylation and retinoic acid receptor β
 DNA methylation as novel targets for gastric cancer
 therapy
 AUTHOR(S): Tahara, Eiichi
 CORPORATE SOURCE: Hiroshima Cancer Seminar Foundation, Radiation Effects
 Research Foundation, Hiroshima University, Minami-ku,
 Horoshima, 732-0815, Japan
 SOURCE: Drug News & Perspectives (2002), 15(9),
 581-585
 CODEN: DNPEED; ISSN: 0214-0934
 PUBLISHER: Prous Science
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English
 AB A review. Multiple genetic and epigenetic alterations in oncogenes,
 tumor-suppressor genes, cell-cycle regulators, cell adhesion mols. and DNA
 repair genes, as well as genetic instability and telomerase activation,
 are responsible for tumor genesis and progression of gastric cancer. The
 scenario of these epigenetic alterations found in gastric cancer differs,
 depending on the two types of gastric cancer, indicating that there are at
 least two types of CpG (cytidine phosphate guanosine) island methylator
 phenotypes in the intestinal-type and diffuse-type of gastric cancer. In
 addition to promoter methylation, acetylated histone H4 is obviously reduced
 in a majority of gastric carcinomas. Histone H4 is progressively
 deacetylated from the early stage (precancerous lesions) to the late stage
 (invasion and metastasis) in gastric carcinogenesis. Since there is no
 difference in the level of acetylated histone H4 between the
 intestinal-type and diffuse-type of gastric cancer, histone H4
 deacetylation may be involved in both types of gastric cancer. This
 review proposes histone acetylation and retinoic acid receptor β DNA
 methylation as novel targets for gastric cancer therapy.
 IT 149647-78-9, Suberoylanilide hydroxamic acid
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (histone acetylation and retinoic acid receptor β (RAR β) DNA
 methylation as novel targets for gastric cancer therapy)
 RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibition; histone acetylation and retinoic acid receptor β
 (RAR β) DNA methylation as novel targets for gastric cancer
 therapy)
 RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 34 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:869074 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 137:363085

TITLE: Treatment of neurodegenerative, psychiatric, and other
nervous system disorders associated with polyglutamine
expansion using histone deacetylase inhibitors

INVENTOR(S): Steffan, Joan S.; Thompson, Leslie M.; Marsh, J.
Lawrence; Bodai, Laszlo; Pallos, Judit

PATENT ASSIGNEE(S): The Regents of the University of California, USA

SOURCE: PCI Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

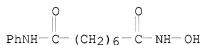
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

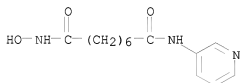
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| WO 2002090534 | A1 | 20021114 | WO 2002-US14167 | 20020502 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002340745 | A1 | 20021118 | AU 2002-340745 | 20020502 <-- |
| EP 1390491 | A1 | 20040225 | EP 2002-769340 | 20020502 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 20040142859 | A1 | 20040722 | US 2003-476627 | 20031030 <-- |
| US 20050227915 | A1 | 20051013 | US 2004-768292 | 20040129 <-- |
| PRIORITY APPLN. INFO.: | | | US 2001-288215P | P 20010502 <-- |
| | | | US 2002-372724P | P 20020411 <-- |
| | | | WO 2002-US14167 | W 20020502 <-- |
| | | | US 2003-443717P | P 20030129 |
| | | | US 2003-476627 | A2 20031030 |

AB The invention relates to a novel method for treating a variety of diseases and disorders, including polyglutamine expansion diseases such as Huntington's disease, neurol. degeneration, psychiatric disorders, and protein aggregation disorders and diseases, comprising administering to patients in need thereof of a therapeutically effective amount of one or more deacetylase inhibitors. Specifically, histone deacetylases are targeted to limit the consequences of aberrant interaction between polyglutamine expansion variants of proteins and transcription factors, such as p53, to prevent aberrant gene expression. The invention is also directed to a transgenic fly useful as a model of polyglutamine expansion diseases, which may be used to test potential therapeutic agents.

IT 149647-78-9, SAHA 382180-17-8, Pyroxamide
RL: ANT (Analyte); BSU (Biological study, unclassified); THU
(Therapeutic use); ANST (Analytical study); BIOL (Biological study);
USES (Uses)
(for treating neurodegenerative disease; treatment of
neurodegenerative, psychiatric, and other nervous system disorders
associated with polyglutamine expansion using histone deacetylase
inhibitors)
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



RN 382180-17-8 CAPLUS
CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; treatment of neurodegenerative, psychiatric, and other
nervous system disorders associated with polyglutamine expansion using
histone deacetylase inhibitors)
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

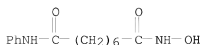
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 35 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:832643 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 137:304765
TITLE: Compositions and methods for reestablishing gene
transcription through inhibition of DNA methylation
and histone deacetylase
INVENTOR(S): Dimartino, Jorge
PATENT ASSIGNEE(S): Supergen, Inc., USA
SOURCE: PCI Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

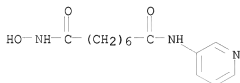
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|----------|-----------------|-----------------|
| WO 2002085400 | A1 | 20021031 | WO 2002-US12092 | 20020419 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 20040204339 | A1 | 20041014 | US 2001-841744 | 20010424 <-- |
| US 6905669 | B2 | 20050614 | | |
| CA 2443560 | A1 | 20021031 | CA 2002-2443560 | 20020419 <-- |
| AU 2002303376 | A1 | 20021105 | AU 2002-303376 | 20020419 <-- |
| EP 1389127 | A1 | 20040218 | EP 2002-731396 | 20020419 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 20050159347 | A1 | 20050721 | US 2005-82130 | 20050315 <-- |
| US 7276228 | B2 | 20071002 | | |
| PRIORITY APPLN. INFO.: | | | US 2001-841744 | A1 20010424 <-- |
| | | | WO 2002-US12092 | W 20020419 <-- |
| AB | Comps. and methods are provided for treating diseases associated with aberrant silencing of gene expression such as cancer by reestablishing the gene expression through inhibition of DNA hypomethylation and histone deacetylase. The method comprises: administering to a patient suffering from the disease a therapeutically effective amount of a DNA methylation inhibitor such as a cysteine analog such as decitabine, in combination with an effective amount of histone deacetylase inhibitor such as hydroxamic acid, cyclic peptide, benzamide, butyrate, and depudecin. | | | |
| IT | 9076-57-7, Histone deacetylase RL: BSU (Biological study, unclassified); BIOL (Biological study) (comps. and methods for reestablishing gene transcription through inhibition of DNA methylation and histone deacetylase for treatment of diseases such as cancer) | | | |
| RN | 9076-57-7 CAPLUS | | | |
| CN | Deacetylase, histone (CA INDEX NAME) | | | |
| *** STRUCTURE DIAGRAM IS NOT AVAILABLE *** | | | | |
| IT | 149647-78-9, SAHA 382180-17-8, Pyroxamide RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (comps. and methods for reestablishing gene transcription through inhibition of DNA methylation and histone deacetylase for treatment of diseases such as cancer) | | | |
| RN | 149647-78-9 CAPLUS | | | |
| CN | Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME) | | | |



RN 382180-17-8 CAPLUS

CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 36 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:651684 CAPLUS <LOGINID:20080505>>

DOCUMENT NUMBER: 138:198269

TITLE: Suberoylanilide hydroxamic acid (SAHA), a histone deacetylase inhibitor, suppresses the growth of carcinogen-induced mammary tumors

AUTHOR(S): Cohen, Leonard A.; Marks, Paul A.; Rifkind, Richard A.; Amin, Shantu; Desai, Dhimant; Pittman, Brian; Richon, Victoria M.

CORPORATE SOURCE: American Health Foundation, Valhalla, NY, 10595, USA

SOURCE: Anticancer Research (2002), 22(3), 1497-1504

CODEN: ANTRD4; ISSN: 0250-7005

PUBLISHER: International Institute of Anticancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Suberoylanilide hydroxamic acid (SAHA), a histone deacetylase inhibitor, was shown to inhibit the development of N-methylnitrosourea (NMU)-induced rat mammary tumors when fed in the diet continuously for the duration of the carcinogenic process. The present study was designed to determine whether the inhibitory effects of SAHA occur during the initiation process or at subsequent stages in the carcinogenic process. In addition, animals with established NMU tumors were administered SAHA to determine whether SAHA could inhibit the continued growth of established mammary tumors. It was found that SAHA fed at 900 ppm in the diet inhibited tumor yields when administered from 14 days prior to NMU administration to termination (-14 to +130) and from +14 and +28 days to termination. However, SAHA had no effect on tumor yields when administered from -14 to +14 or from -14 to +50 days and then returned to the control diets for the remainder of the exptl. period (130 days). These results indicate that the inhibitory effects of SAHA are not exerted at the initiation phase of NMU-induced mammary tumorigenesis and appear, instead, to inhibit the subsequent stages in tumor development. Of most interest was the ability of SAHA to inhibit the growth of established mammary tumors. Administration, of SAHA in the diet at 900 ppm resulted in significant inhibition of established tumor growth. Thirty-two percent of SAHA-treated tumors exhibited partial regression compared to 12% of controls, growth was stabilized in 24% of treated tumors compared to 12% of controls while 11% exhibited complete regression compared to 0% of controls. Collectively, SAHA-treated tumors exhibited a 7 fold reduction in growth compared to untreated tumors over the

test period. The results of this animal model study indicate that SAHA, when fed in the diet, serves as both a chemopreventive and chemotherapeutic agent in the absence of any detectable side effects.

IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; suberoylanilide hydroxamic acid, a histone deacetylase inhibitor, suppresses growth of mammary tumors)

RN 9076-57-7 CAPLUS

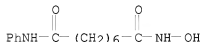
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, SAHA
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (suberoylanilide hydroxamic acid, a histone deacetylase inhibitor, suppresses growth of mammary tumors)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 37 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:594666 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 137:135074

TITLE: Use of retinoids plus histone deacetylase inhibitors to inhibit the growth of solid tumors

INVENTOR(S): Gudas, Lorraine J.; Nanus, David

PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA

SOURCE: PCT Int. Appl., 40 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

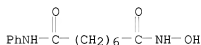
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 2002060430 | A1 | 20020808 | WO 2002-US2976 | 20020201 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002242057 | A1 | 20020812 | AU 2002-242057 | 20020201 <-- |

US 20020183388 A1 20021205 US 2002-61101 20020201 <--
PRIORITY APPLN. INFO.: US 2001-265651P P 20010201 <--
WO 2002-US2976 W 20020201 <--
AB The invention provides a method of inhibiting growth of solid tumors in an animal which comprises administering an effective amount of trichostatin A to an animal in need of such treatment. The invention also provides a method of inhibiting growth of solid tumors in an animal which comprises administering an effective amount of a histone deacetylase inhibitor and a retinoid to an animal in need of such treatment. Examples of solid tumors which may be treated using the methods of the invention include but are not limited to carcinomas of the head and neck, breast, skin, kidney, oral cavity, colon, prostate, pancreas and lung.
IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (retinoids and histone deacetylase inhibitors for inhibition of growth of solid tumors)
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT 149647-78-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (retinoids and histone deacetylase inhibitors for inhibition of growth of solid tumors)
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 38 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:539823 CAPLUS <LOGINID:20080505>
DOCUMENT NUMBER: 137:103874
TITLE: Histone deacetylase inhibitors enhancing iodide or iodine uptake and uses in diagnosis and treatment of thyroid neoplasms
INVENTOR(S): Fojo, Antonio Tito; Bates, Susan Elaine
PATENT ASSIGNEE(S): The Government of the United States of America, Department of Health & Human Services, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|-------|-----------------|-------|
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WO 2002055688 A2 20020718 WO 2002-US714 20020108 <--
 WO 2002055688 A3 20030410
 WO 2002055688 A8 20030925
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
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 LS, LI, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
 GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
 GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2002249938 A1 20020724 AU 2002-249938 20020108 <--
 CA 2434269 A1 20020718 CA 2002-2434269 20020109 <--
 EP 1356053 A2 20031029 EP 2002-718823 20020109 <--
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2005507231 T 20050317 JP 2002-556736 20020109 <--
 US 20040132643 A1 20040708 US 2004-250320 20040102 <--
 PRIORITY APPLN. INFO.: US 2001-260733P P 20010110 <--
 WO 2002-US714 W 20020108 <--

AB Disclosed herein are novel approaches to thyroid cancer therapy. These approaches include methods to enhance thyroid specific gene expression, for example methods to enhance expression of thyroglobulin and/or the Na⁺/I⁻ symporter in thyroid cancer cells. Enhanced expression of thyroid-specific genes promotes cellular differentiation and reduces biol. aggressive behavior such as invasion and metastasis. In addition, enhanced expression of thyroglobulin and/or the Na⁺/I⁻ symporter increases the ability of thyroid cancer cells to concentrate iodine or iodide, thereby making the cells more susceptible to radioactive iodine therapy. Also disclosed herein are methods for detecting thyroid neoplasms in a subject, by administering a therapeutically effective amount of a histone deacetylase inhibitor, administering a detectable agent whose uptake or concentration in thyroid cells is increased by administration of the histone deacetylase inhibitor, and detecting the detectable agent.

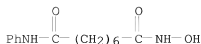
IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (histone deacetylase inhibitors enhancing iodide or iodine uptake and uses in diagnosis and treatment of thyroid neoplasms)

RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (histone deacetylase inhibitors enhancing iodide or iodine uptake and uses in diagnosis and treatment of thyroid neoplasms)

RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



L42 ANSWER 39 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2002:539476 CAPLUS <<LOGINID::20080505>>
 DOCUMENT NUMBER: 137:88450
 TITLE: Method of treating autoimmune diseases with histone
 hyperacetylating agent
 INVENTOR(S): Kammer, Gary M.; Mishra, Nilamadhab
 PATENT ASSIGNEE(S): Wake Forest University, USA
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|--|----------|-----------------|--------------|
| WO 2002055017 | A2 | 20020718 | WO 2001-US43871 | 20011119 <-- |
| WO 2002055017 | A3 | 20030123 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2002243231 | A1 | 20020724 | AU 2002-243231 | 20011119 <-- |
| US 20030114525 | A1 | 20030619 | US 2002-151481 | 20020520 <-- |
| US 7271198 | B2 | 20070918 | | |
| US 20030082666 | A1 | 20030501 | US 2002-187586 | 20020702 <-- |
| US 20060178437 | A1 | 20060810 | US 2006-403608 | 20060413 <-- |

PRIORITY APPLN. INFO.:

| | | |
|-----------------|----|--------------|
| US 2000-718195 | A | 20001120 <-- |
| WO 2001-US43871 | W | 20011119 <-- |
| US 2002-187586 | A3 | 20020702 <-- |

AB A method of treating an autoimmune disease (for example, Systemic Lupus Erythematosus) comprises administering to the subject a treatment effective amount of a histone hyperacetylating agent, or a pharmaceutically acceptable salt thereof. Methods of screening compds. useful for the treatment of autoimmune disease are also disclosed. Trichostatin A down-regulated CD154 and interleukin 10 and up-regulated interferon- γ in SLE T cells.

IT 9076-57-7, Histone deacetylase
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (inhibitor; method of treating autoimmune diseases with histone hyperacetylating agent)

RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

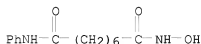
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(method of treating autoimmune diseases with histone hyperacetylating agent)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



L42 ANSWER 40 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:496846 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 138:198218

TITLE: Synergistic induction of mitochondrial damage and apoptosis in human leukemia cells by flavopiridol and the histone deacetylase inhibitor suberoylanilide hydroxamic acid (SAHA)

AUTHOR(S): Almenara, J.; Rosato, R.; Grant, S.

CORPORATE SOURCE: Medical College of Virginia, Department of Medicine, Virginia Commonwealth University, Richmond, VA, USA

SOURCE: Leukemia (2002), 16(7), 1331-1343

CODEN: LEUKED; ISSN: 0887-6924

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Interactions between the histone deacetylase inhibitor SAHA (suberoylanilide hydroxamic acid) and the cyclin-dependent kinase (CDK) inhibitor flavopiridol (FP) were examined in human leukemia cells. Simultaneous exposure (24 h) of myelomonocytic leukemia cells (U937) to SAHA (1 μM) and FP (100 nM), which were minimally toxic alone (1.5 and 16.3% apoptosis resp.), produced a dramatic increase in cell death (ie 63.2% apoptotic), reflected by morphol., procaspase-3 and -8 cleavage, Bid activation, diminished ΔWm , and enhanced cytochrome c release. FP blocked SAHA-mediated up-regulation of p21CIP1 and CD11b expression, while inducing caspase-dependent Bcl-2 and pRb cleavage. Similar interactions were observed in HL-60 and Jurkat leukemic cells. Enhanced apoptosis in SAHA/FP-treated cells was accompanied by a marked reduction in clonogenic survival. Ectopic expression of either dominant-neg. caspase-8 (C8-DN) or CrmA partially attenuated SAHA/FP-mediated apoptosis (eg 45 and 38.2% apoptotic vs 78% in controls) and Bid cleavage. SAHA/FP induced apoptosis was unaffected by the free radical scavenger L-N-acetyl Cys or the PKC inhibitor GFX. Finally, ectopic Bcl-2 expression marginally attenuated SAHA/FP-related apoptosis/cytochrome c release, and failed to restore clonogenicity in cells exposed to these agents. Together, these findings indicate that SAHA and FP interact synergistically to induce mitochondrial damage and apoptosis in human leukemia cells, and suggest that this process may also involve engagement of the caspase-8-dependent apoptotic cascade.

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; synergistic interaction of flavopiridol and SAHA in leukemia)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, SAHA

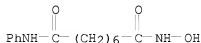
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(synergistic interaction of flavopiridol and SAHA in leukemia)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 41 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:462894 CAPLUS <<LOGINID::20080505>>

DOCUMENT NUMBER: 137:179388

TITLE: Structure-Activity Relationships on Phenylalanine-Containing Inhibitors of Histone Deacetylase: In Vitro Enzyme Inhibition, Induction of Differentiation, and Inhibition of Proliferation in Friend Leukemic Cells

AUTHOR(S): Wittich, Sybille; Scherf, Hans; Xie, Changping; Brosch, Gerald; Loidl, Peter; Gerhaeuser, Clarissa; Jung, Manfred

CORPORATE SOURCE: Department of Pharmaceutical and Medicinal Chemistry, Westfaelische Wilhelms-Universitaet Muenster, Muenster, 48149, Germany

SOURCE: Journal of Medicinal Chemistry (2002), 45(15), 3296-3309

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

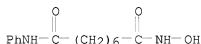
OTHER SOURCE(S): CASREACT 137:179388

AB Inhibitors of histone deacetylases (HDACs) are a new class of anticancer agents that affect gene regulation. We had previously reported the first simple synthetic HDAC inhibitors with in vitro activity at submicromolar concns. Here, we present structure-activity data on modifications of a phenylalanine-containing lead compound including amino acid amides as well as variations of the amino acid part. The compds. were tested for inhibition of maize HD-2, rat liver HDAC, and for the induction of terminal cell differentiation and inhibition of proliferation in Friend leukemic cells. In the amide series, in vitro inhibition was potentiated up to 15-fold, but the potential to induce cell differentiation decreased. Interestingly, an HDAC class selectivity was indicated among some of these amides. In the amino acid Me ester series, a biphenylalanine derivative was identified as a good enzyme inhibitor, which blocks proliferation in the submicromolar range and is also a potent inducer of terminal cell differentiation.

IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and structure-activity relationships on
phenylalanine-containing
inhibitors of histone deacetylase in Friend leukemic cells)
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, SAHA
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(preparation and structure-activity relationships on
phenylalanine-containing
inhibitors of histone deacetylase in Friend leukemic cells)
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 42 OF 56 CAPLUS COPYRIGHT 2008 ACS ON STN
ACCESSION NUMBER: 2002:298819 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 137:210564
TITLE: Suberoylanilide hydroxamic acid (SAHA) overcomes
multidrug resistance and induces cell death in
P-glycoprotein-expressing cells
AUTHOR(S): Ruefli, Astrid A.; Bernhard, David; Tainton, Kellie
M.; Kofler, Reinhard; Smyth, Mark J.; Johnstone, Ricky
W.
CORPORATE SOURCE: Cancer Immunology Division, The Peter MacCallum Cancer
Institute, East Melbourne, 3002, Australia
SOURCE: International Journal of Cancer (2002),
99(2), 292-298
CODEN: IJCNW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Multidrug resistance (MDR) mediated by the ATP-dependent efflux protein
P-glycoprotein (P-gp) is a major obstacle to the successful treatment of
many cancers. In addition to effluxing toxins, P-gp has been shown to
protect tumor cells against caspase-dependent apoptosis mediated by Fas
and tumor necrosis factor receptor (TNFR) ligation, serum starvation and
UV irradiation. However, P-gp does not protect against caspase-independent
cell death mediated by granzyme B or pore-forming proteins (perforin,
pneumolysin and activated complement). The authors examined the effects of
the chemotherapeutic hybrid polar compound suberoylanilide hydroxamic acid
(SAHA) on P-gp-expressing MDR human tumor cell lines. In the CEM T-cell
line, SAHA, a histone deacetylase inhibitor, induced equivalent death in

P-gp-pos. cells compared with P-gp-neg. cells. Cell death was marked by the caspase-independent release of cytochrome c, reactive oxygen species (ROS) production and Bid cleavage that was not affected by P-gp expression. However, consistent with the authors' previous findings, SAHA-induced caspase activation was inhibited in P-gp-expressing cells. These data provide evidence that P-gp inhibits caspase activation after chemotherapeutic drug treatment and demonstrates that SAHA may be of value for the treatment of P-gp-expressing MDR cancers.

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; suberoylanilide hydroxamic acid overcomes

P-glycoprotein-mediated multidrug resistance and induces cell death human tumor cells and mechanism involved)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

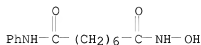
IT 149647-78-9, SAHA

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(suberoylanilide hydroxamic acid overcomes P-glycoprotein-mediated multidrug resistance and induces cell death human tumor cells and mechanism involved)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 43 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:256222 CAPLUS <<LOGINID::20080505>>

DOCUMENT NUMBER: 136:294651

TITLE: Preparation of aryl-substituted N-hydroxy amides with amide linkages as HDAC inhibitors for treatment of proliferative conditions

INVENTOR(S): Watkins, Clare J.; Romero-Martin, Maria-Rosario; Moore, Kathryn G.; Ritchie, James; Finn, Paul W.; Kalvinsh, Ivars; Loza, Einars; Starchenkov, Igor; Dikovska, Klara; Bokaldere, Rasma Melita; Gailite, Viija; Vorona, Maxim; Andrianov, Victor; Lolya, Daina; Semenikhina, Valentina; Amolins, Andris; Harris, C. John; Duffy, James E. S.

PATENT ASSIGNEE(S): Prolifix Limited, UK
SOURCE: PCT Int. Appl., 346 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-----------------|
| WO 2002026696 | A1 | 20020404 | WO 2001-GB4329 | 20010927 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2423868 | A1 | 20020404 | CA 2001-2423868 | 20010927 <-- |
| AU 2001090134 | A | 20020408 | AU 2001-90134 | 20010927 <-- |
| EP 1335898 | A1 | 20030820 | EP 2001-970014 | 20010927 <-- |
| EP 1335898 | B1 | 20051123 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004509941 | T | 20040402 | JP 2002-531082 | 20010927 <-- |
| EP 1598067 | A1 | 20051123 | EP 2005-15737 | 20010927 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | | |
| AT 310719 | T | 20051215 | AT 2001-970014 | 20010927 <-- |
| ES 2257441 | T3 | 20060801 | ES 2001-970014 | 20010927 <-- |
| US 20040092598 | A1 | 20040513 | US 2003-381791 | 20030827 <-- |
| PRIORITY APPLN. INFO.: | | | GB 2000-23985 | A 20000929 <-- |
| | | | US 2001-297785P | P 20010614 <-- |
| | | | EP 2007-970014 | A3 20010927 <-- |
| | | | WO 2001-GB4329 | W 20010927 <-- |

OTHER SOURCE(S): MARPAT 136:294651

AB The title compds. AQLJQ2CONHOH [I; wherein A = aryl group; Q1 = aryl leader group having a backbone of at least 2 C atoms; J = NR1CO or CONR1; R1 = amido substituent; Q2 = acid leader group; and pharmaceutically acceptable salts, solvates, amides, esters, ethers, chemical protected forms, and prodrugs thereof] were prepared via solution phase and solid phase synthetic methods as histone deacetylase (HDAC) inhibitors for treatment of proliferative conditions, such as cancer and psoriasis. For example, 6-aminocaproic acid Me ester•HCl was coupled with 2-naphthoyl chloride in the presence of diisopropyl ethylamine in DMF to give the amide. Deesterification (79%), followed by conversion to the N-hydroxyamide using HONH2•HCl in the presence of 1,1'-carbonyldiimidazole in THF, afforded naphthalene-2-carboxylic acid (5-hydroxycarbamoylpentyl)amide II (PX105687) in 40% yield. The latter inhibited recombinant HDAC1 and HDAC2 with IC50 values of 33 nM and 29 nM, resp., and inhibited cell proliferation against the human cervical adenocarcinoma (HeLa) cell line using cell proliferation reagent WST-1 with IC50 of 1.1 nM. Structure-activity relationship studies showed superior activity for I when (1) the backbone of Q1 had > 1 carbon atoms, and (2) the alkylene group Q2 had > 5 carbon atoms.

IT 408357-61-9P, PX 116218 408357-69-7P, PX 116223 408357-72-2P, PX 117720

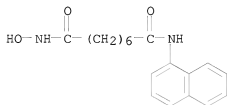
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(HDAC inhibitor; preparation of N-hydroxy amides with amide linkages as HDAC

inhibitors for treatment of proliferative conditions)

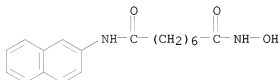
RN 408357-61-9 CAPLUS

CN Octanediamide, N-hydroxy-N'-1-naphthalenyl- (9CI) (CA INDEX NAME)



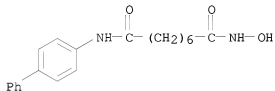
RN 408357-69-7 CAPLUS

CN Octanediamide, N-hydroxy-N'-2-naphthalenyl- (9CI) (CA INDEX NAME)



RN 408357-72-2 CAPLUS

CN Octanediamide, N-[1,1'-biphenyl]-4-yl-N'-hydroxy- (9CI) (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(preparation of N-hydroxy amides with amide linkages as HDAC inhibitors for treatment of proliferative conditions)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT:

6

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 44 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:224891 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 137:72839

TITLE: The antitumor histone deacetylase inhibitor

suberoylanilide hydroxamic acid exhibits antiinflammatory properties via suppression of cytokines

AUTHOR(S): Leonì, Flavio; Zaliani, Andrea; Bertolini, Giorgio; Porro, Giulia; Pagani, Paolo; Pozzi, Pietro; Dona, Giancarlo; Fossati, Gianluca; Sozzani, Silvano; Azam, Tania; Bufler, Philip; Fantuzzi, Giampaolo; Goncharov, Igor; Kim, Soo-Hyun; Pomerantz, Benjamin J.; Reznikov, Leonid L.; Siegmund, Britta; Dinarello, Charles A.; Mascagni, Paolo

CORPORATE SOURCE: Italfarmaco, SpA., Balsamo, 20092, Italy

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(5), 2995-3000

CODEN: PNAS6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Suberoylanilide hydroxamic acid (SAHA) is a hydroxamic acid-containing hybrid polar mol.; SAHA specifically binds to and inhibits the activity of histone deacetylase. Although SAHA, like other inhibitors of histone deacetylase, exhibits antitumor effects by increasing expression of genes regulating tumor survival, we found that SAHA reduces the production of proinflammatory cytokines in vivo and in vitro. A single oral administration of SAHA to mice dose-dependently reduced circulating TNF- α , IL-1 β , IL-6, and IFN- γ induced by lipopolysaccharide (LPS). Administration of SAHA also reduced hepatic cellular injury in mice following i.v. injection of Con A. SAHA inhibited nitric oxide release in mouse macrophages stimulated by the combination of TNF- α plus IFN- γ . Human peripheral blood mononuclear cells stimulated with LPS in the presence of SAHA released less TNF- α , IL-1 β , IL-12, and IFN- γ (50% reduction at 100-200 nM). The production of IFN- γ stimulated by IL-18 plus IL-12 was also inhibited by SAHA (85% at 200 nM). However, SAHA did not affect LPS-induced synthesis of the IL-1 β precursor, the IL-1 receptor antagonist, or the chemokine IL-8. In addition, IFN- γ induced by anti-CD3 was not suppressed by SAHA. Steady-state mRNA levels for LPS-induced TNF- α and IFN- γ in peripheral blood mononuclear cells were markedly decreased, whereas IL-8 and IL-1 β mRNA levels were unaffected. Because SAHA exhibits antiinflammatory properties in vivo and in vitro, inhibitors of histone deacetylase may stimulate the expression of genes that control the synthesis of cytokines and nitric oxide or hyper-acetylate other targets.

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (antitumor histone deacetylase inhibitor suberoylanilide hydroxamic acid exhibits antiinflammatory properties via suppression of cytokines)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

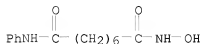
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antitumor histone deacetylase inhibitor suberoylanilide hydroxamic acid exhibits antiinflammatory properties via suppression of cytokines)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 45 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2002:220378 CAPLUS <<LOGINID:20080505>>
 DOCUMENT NUMBER: 136:241653
 TITLE: Promotion of apoptosis in cancer cells by

INVENTOR(S): co-administration of cyclin dependent kinase inhibitors and cellular differentiation agents
 Grant, Steven; Dent, Paul; Rosato, Roberto; Cartee, Leanne

PATENT ASSIGNEE(S): Virginia Commonwealth University, USA

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------------|
| WO 2002022133 | A1 | 20020321 | WO 2001-US28297 | 20010907 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001087157 | A5 | 20020326 | AU 2001-87157 | 20010907 <-- |
| US 20050004007 | A1 | 20050106 | US 2003-363540 | 20030305 <-- |
| PRIORITY APPLN. INFO.: | | | US 2000-231885P | P 20000912 <-- |
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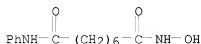
AB The invention provides compns. and methods for promoting apoptosis of cancer cells, and methods for treating cancer. The compns. comprise cyclin dependent kinase inhibitor and an agent that induces cellular differentiation. The methods of promoting apoptosis of cancer cells involve the co-administration to the cancer cells of a cyclin dependent kinase inhibitor and an agent that induces cell differentiation. The method for treating cancer involves the co-administration of a cyclin dependent kinase inhibitor and an agent that induces cellular differentiation to a patient. Examples of cellular differentiation agents include histone deacetylase inhibitors, protein kinase C activators, retinoids, and Vitamin D3.

IT 149647-78-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitor; promotion of apoptosis in cancer cells by co-administration of cyclin dependent kinase inhibitors and cellular differentiation agents)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; promotion of apoptosis in cancer cells by co-administration of cyclin dependent kinase inhibitors and cellular differentiation agents)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 46 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:108360 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 136:395648

TITLE: Histone deacetylases inhibitors as anti-angiogenic agents altering vascular endothelial growth factor signaling

AUTHOR(S): Deroanne, Christophe F.; Bonjean, Karine; Servotte, Sandrine; Devy, Laetitia; Colige, Alain; Clausse, Nathalie; Blacher, Sylvia; Verdin, Eric; Foidart, Jean-Michel; Nusgens, Betty V.; Castronovo, Vincent

CORPORATE SOURCE: Research Center in Experimental Cancerology, Laboratory of Connective Tissues Biology, University of Liege, Liege, B-4000, Belg.

SOURCE: Oncogene (2002), 21(3), 427-436

CODEN: OCNES; ISSN: 0950-9232

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

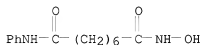
AB Angiogenesis is a complex biol. process involving the coordinated modulation of many genes. Histone deacetylases (HDAC) are a growing family of enzymes that mediate the availability of chromatin to the transcriptional machinery. Trichostatin-A (TSA) and suberoylanilide hydroxamic acid (SAHA), two HDAC inhibitors known to relieve gene silencing, were evaluated as potential antiangiogenic agents. TSA and SAHA were shown to prevent vascular endothelial growth factor (VEGF)-stimulated human umbilical cord endothelial cells (HUEVC) from invading a type I collagen gel and forming capillary-like structures. SAHA and TSA inhibited the VEGF-induced formation of a CD31-pos. capillary-like network in embryoid bodies and inhibited the VEGF-induced

angiogenesis in the CAM assay. TSA also prevented, in a dose-response relation, the sprouting of capillaries from rat aortic rings. TSA inhibited in a dose-dependent and reversible fashion the VEGF-induced expression of VEGF receptors, VEGFR1, VEGFR2, and neuropilin-1. TSA and SAHA upregulated the expression by HUVEC of semaphorin III, a recently described VEGF competitor, at both mRNA and protein levels. This effect was specific to endothelial cells and was not observed in human fibroblasts neither in vascular smooth muscle cells. These observations provide a conspicuous demonstration that HDAC inhibitors are potent anti-angiogenic factors altering VEGF signaling.

IT 9076-57-7, Histone deacetylase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (histone deacetylases inhibitors as anti-angiogenic agents altering
 vascular endothelial growth factor signaling)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (histone deacetylases inhibitors as anti-angiogenic agents altering
 vascular endothelial growth factor signaling)
 RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 47 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2002:9423 CAPLUS <<LOGINID:20080505>>
 DOCUMENT NUMBER: 136:241518
 TITLE: Histone deacetylase inhibitors reduce polyglutamine toxicity
 AUTHOR(S): McCampbell, Alexander; Taye, Addis A.; Whitty, Leslie; Penney, Ellen; Steffan, Joan S.; Fischbeck, Kenneth H.
 CORPORATE SOURCE: Neurogenetics Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, 20892, USA
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(26), 15179-15184
 CODEN: PNASA6; ISSN: 0027-8424
 PUBLISHER: National Academy of Sciences
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Polyglutamine diseases include at least nine neurodegenerative disorders, each caused by a CAG repeat expansion in a different gene. Accumulation of mutant polyglutamine-containing proteins occurs in patients, and evidence

from cell culture and animal expts. suggests the nucleus as a site of pathogenesis. To understand the consequences of nuclear accumulation, the authors created a cell culture system with nuclear-targeted polyglutamine. In the authors system, cell death can be mitigated by overexpression of full-length cAMP response element binding protein (CREB)-binding protein (CBP) or its amino-terminal portion alone. CBP is one of several histone acetyltransferases sequestered by polyglutamine inclusions. The authors found histone acetylation to be reduced in cells expressing mutant polyglutamine. Reversal of this hypoacetylation, which can be achieved either by overexpression of CBP or its amino terminus or by treatment with deacetylase inhibitors, reduced cell loss. These findings suggest that nuclear accumulation of polyglutamine can lead to altered protein acetylation in neurons and indicate a novel therapeutic strategy for polyglutamine disease.

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(histone deacetylase inhibitors reduce polyglutamine toxicity in neurons in relation to CBP transcription factor expression)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

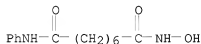
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors reduce polyglutamine toxicity in neurons in relation to CBP transcription factor expression)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 48 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:914781 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 136:193822

TITLE: The histone deacetylase inhibitor suberoylanilide hydroxamic acid induces differentiation of human breast cancer cells

AUTHOR(S): Munster, Pamela N.; Troso-Sandoval, Tiffany; Rosen, Neal; Rifkind, Richard; Marks, Paul A.; Richon, Victoria M.

CORPORATE SOURCE: Program in Cell Biology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA

SOURCE: Cancer Research (2001), 61(23), 8492-8497

CODEN: CNREAB; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Histone deacetylase (HDACs) regulate histone acetylation by catalyzing the removal of acetyl groups on the NH₂-terminal lysine residues of the core nucleosomal histones. Modulation of the acetylation status of core histones is involved in the regulation of the transcriptional activity of certain genes. HDAC activity is generally associated with transcriptional repression. Aberrant recruitment of HDAC activity has been associated with the development of certain human cancers. We have developed a class of HDAC inhibitors, such as suberoylanilide hydroxamic acid (SAHA), that were initially identified based on their ability to induce differentiation of cultured murine erythroleukemia cells. Addnl. studies have demonstrated that SAHA inhibits the growth of tumors in rodents. In this study we have examined the effects of SAHA on MCF-7 human breast cancer cells. We found that SAHA causes the inhibition of proliferation, accumulation of cells in a dose-dependent manner in G1 then G2-M phase of the cell cycle, and induction of milk fat globule protein, milk fat membrane globule protein, and lipid droplets. Growth inhibition was associated with morphol. changes including the flattening and enlargement of the cytoplasm, and a decrease in the nuclear: cytoplasmic ratio. Withdrawal of SAHA led to reentry of cells into the cell cycle and reversal to a less differentiated phenotype. SAHA induced differentiation in the estrogen receptor-neg. cell line SKBr-3 and the retinoblastoma-neg. cell line MDA-468. We propose that SAHA has profound antiproliferative activity by causing these cells to undergo cell cycle arrest and differentiation that is dependent on the presence of SAHA. SAHA and other HDAC inhibitors are currently in Phase I clin. trials. These findings may impact the clin. use of these drugs.

IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(histone deacetylase inhibitor suberoylanilide hydroxamic acid induces differentiation of human breast cancer cells)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

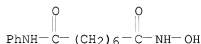
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9, SAHA

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(histone deacetylase inhibitor suberoylanilide hydroxamic acid induces differentiation of human breast cancer cells)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

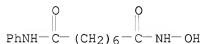
L42 ANSWER 49 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:908905 CAPLUS <LOGINID:20080505>>

DOCUMENT NUMBER: 137:87961

TITLE: Histone deacetylase inhibitors induce

caspace-dependent apoptosis and downregulation of daxx in acute promyelocytic leukaemia with t(15;17)
Amin, Hesham M.; Saeed, Shahnaz; Alkan, Serhan
Department of Pathology, Loyola University Medical Center, Maywood, IL, 60153, USA
SOURCE: British Journal of Haematology (2001), 115(2), 287-297
CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Histone deacetylase (HDAC) appears to play an important role in the pathogenesis of acute promyelocytic leukemia (APL) as it is recruited by both PML-RAR α and PLZF/RAR α in leukemic cells with t(15;17) and t(11;17), resp. Recent studies have demonstrated that HDAC inhibitors can be therapeutically used in various neoplastic disorders including APL. Cell differentiation was considered the major mechanism of the anti-leukemic effects of HDAC inhibitors in APL. However, most of these studies either evaluated the effect of HDAC inhibitors in combination with all-trans retinoic acid (ATRA) or focused on the less common form of APL with t(11;17). To investigate the cellular effects of HDAC inhibitors, including sodium butyrate, trichostatin A, and suberoylanilide hydroxamic acid (SAHA), we used two APL cell lines, NB4 and the ATRA-resistant derivative NB4.306. Moreover, primary cells from five patients with cytogenetic evidence for t(15;17) were also studied. Our results demonstrated that HDAC inhibitors induce distinct caspase-dependent apoptosis in APL, which showed both concentration- and time-dependence. In addition, changes in the apoptosis-regulatory proteins, daxx, bcl-2 and bax were analyzed. HDAC inhibitors induced downregulation of daxx, but no significant changes were detected in bcl-2 or bax. In conclusion, apoptosis induced by HDAC inhibitors in APL could provide an effective strategy for treatment of patients with t(15;17).
IT 149647-78-9, SAHA
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors induce caspase-dependent apoptosis and downregulation of daxx in acute promyelocytic leukemia with t(15;17))
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)

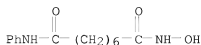


IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; histone deacetylase inhibitors induce caspase-dependent apoptosis and downregulation of daxx in acute promyelocytic leukemia with t(15;17))
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 50 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:867915 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 137:72300
TITLE: Histone deacetylase inhibitors as new cancer drugs
AUTHOR(S): Marks, Paul A.; Richon, Victoria M.; Breslow, Ronald; Rifkind, Richard A.
CORPORATE SOURCE: Cell Biology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Current Opinion in Oncology (2001), 13(6), 477-483
CODEN: CUOOE8; ISSN: 1040-8746
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Histone deacetylase inhibitors are potent inducers of growth arrest, differentiation, or apoptotic cell death in a variety of transformed cells in culture and in tumor bearing animals. Histone deacetylases and the family of histone acetyl transferases are involved in determining the acetylation of histones, which play a role in regulation of gene expression. Radiograph crystallog. studies reveal that the histone deacetylase inhibitors, suberoylanilide hydroxamic acid and trichostatin A, fit into the catalytic site of histone deacetylase, which has a tubular structure with a zinc atom at its base. The hydroxamic acid moiety of the inhibitor binds to the zinc. Histone deacetylase inhibitors cause acetylated histones to accumulate in both tumor and peripheral circulating mononuclear cells. Accumulation of acetylated histones has been used as a marker of the biol. activity of the agents. Hydroxamic acid-based histone deacetylase inhibitors limit tumor cell growth in animals with little or no toxicity. These compds. act selectively on genes, altering the transcription of only approx. 2% of expressed genes in cultured tumor cells. A number of proteins other than histones are substrates for histone deacetylases. The role that these other targets play in histone deacetylase inducement of cell growth arrest, differentiation, or apoptotic cell death is not known. This review summarizes the characteristics of a variety of inhibitors of histone deacetylases and their effects on transformed cells in culture and tumor growth in animal models. Several structurally different histone deacetylase inhibitors are in phase I or II clin. trials in patients with cancers.
IT 149647-78-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histone deacetylase inhibitors as new cancer drugs)
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; histone deacetylase inhibitors as new cancer drugs)
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 51 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:363640 CAPLUS <<LOGINID::20080505>>

DOCUMENT NUMBER: 136:480/1

TITLE: Inhibition of transformed cell growth and induction of
cellular differentiation by pyroxamide, an inhibitor
of histone deacetylase

AUTHOR(S): Butler, Lisa M.; Webb, Yael; Agus, David B.; Higgins,
Brian; Tolentino, Thomas R.; Kutko, Martha C.;
LaQuaglia, Michael P.; Drobnjak, Marija; Cordon-Cardo,
Carlos; Scher, Howard I.; Breslow, Ronald; Richon,
Victoria M.; Rifkind, Richard A.; Marks, Paul A.

CORPORATE SOURCE: Cell Biology Program, Memorial Sloan-Kettering Cancer
Center, New York, NY, 10021, USA

SOURCE: Clinical Cancer Research (2001), 7(4),
962-970

CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have synthesized a series of hybrid polar compds. that induce
differentiation and/or apoptosis of various transformed cells. These
agents are also potent inhibitors of histone deacetylases (HDACs).
Pyroxamide (suberoyl-3-aminopyridineamide hydroxamic acid) is a new member
of this class of compds. that is currently under development as an
anticancer agent. We investigated the activity of pyroxamide as an
inducer of differentiation and/or apoptosis in transformed cells.
Pyroxamide, at micromolar concns., induced terminal differentiation in
murine erythroleukemia (MEL) cells and caused growth inhibition by cell
cycle arrest and/or apoptosis in MEL, prostate carcinoma, bladder
carcinoma, and neuroblastoma cells. Administration of pyroxamide (100 or
200 mg/kg/day) to nude mice at doses that caused little evident toxicity
significantly suppressed the growth of s.c. CWR22 prostate cancer
xenografts. Despite the potent growth-inhibitory effects of pyroxamide in
this tumor model, serum prostate-specific antigen levels in control vs.
pyroxamide-treated mice were not significantly different. Pyroxamide is a
potent inhibitor of affinity-purified HDAC1 (ID50 = 100 nM) and causes the
accumulation of acetylated core histones in MEL cells cultured with the
agent. Human CWR22 prostate tumor xenografts from mice treated with
pyroxamide (100 or 200 mg/kg/day) showed increased levels of histone
acetylation and increased expression of the cell cycle regulator p21/WAF1,
compared with tumors from vehicle-treated control animals. The findings
suggest that pyroxamide may be a useful agent for the treatment of
malignancy and that induction of p21/WAF1 in transformed cells by
pyroxamide may contribute to the antitumor effects of this agent.

IT 382180-17-8, Pyroxamide

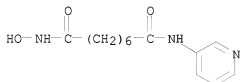
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological

activity); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)

(antitumor effects of pyroxamide, an inhibitor of histone deacetylase)

RN 382180-17-8 CAPLUS

CN Octanediamide, N1-hydroxy-N8-3-pyridinyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(antitumor effects of pyroxamide, an inhibitor of histone deacetylase)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 52 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:185885 CAPLUS <<LOGINID:20080505>>

DOCUMENT NUMBER: 134:237397

TITLE: Preparation of alkanolic acid derivatives as novel
class of cytodifferentiating agents and histone
deacetylase inhibitors, and methods of use thereof
INVENTOR(S): Richon, Victoria M.; Marks, Paul A.; Rifkind, Richard
A.; Breslow, Ronald; Belvedere, Sandro; Gershell,
Leland; Miller, Thomas A.

PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA;
Trustees of Columbia University in the City of New
York

SOURCE: PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 2001018171 | A2 | 20010315 | WO 2000-US23232 | 20000824 <-- |
| WO 2001018171 | A3 | 20020627 | | |
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| HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, | | | | |
| LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, | | | | |
| SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, | | | | |
| ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, | | | | |

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 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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| CA 2383999 | A1 | 20010315 | CA 2000-2383999 | 20000824 <-- |
| AU 2000069327 | A | 20010410 | AU 2000-69327 | 20000824 <-- |
| EP 1231919 | A2 | 20020821 | EP 2000-957757 | 20000824 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| BR 2000014254 | A | 20020827 | BR 2000-14254 | 20000824 <-- |
| HU 2002002707 | A2 | 20021228 | HU 2002-2707 | 20000824 <-- |
| HU 2002002707 | A3 | 20031128 | | |
| US 6511990 | B1 | 20030128 | US 2000-645430 | 20000824 <-- |
| JP 2003509343 | T | 20030311 | JP 2001-522383 | 20000824 <-- |
| NZ 517613 | A | 20040130 | NZ 2000-517613 | 20000824 <-- |
| ZA 2002001544 | A | 20021010 | ZA 2002-1544 | 20020225 <-- |
| MX 2002PA02505 | A | 20040910 | MX 2002-PA2505 | 20020307 <-- |
| US 20040002506 | A1 | 20040101 | US 2002-281875 | 20021025 <-- |
| US 7126001 | B2 | 20061024 | | |
| AU 2005205805 | A1 | 20050929 | AU 2005-205805 | 20050902 <-- |
| US 20060241129 | A1 | 20061026 | US 2006-474043 | 20060622 <-- |
| US 7345174 | B2 | 20080318 | | |
| US 20070010536 | A1 | 20070111 | US 2006-473839 | 20060622 <-- |
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| | | | US 1999-152755P | P 19990908 <-- |
| | | | US 2000-208688P | P 20000601 <-- |
| | | | AU 2000-69327 | A3 20000824 <-- |
| | | | US 2000-645430 | A1 20000824 <-- |
| | | | WO 2000-US23232 | W 20000824 <-- |
| | | | US 2002-281875 | A3 20021025 <-- |

OTHER SOURCE(S): MARPAT 134:237397

AB The present invention provides the compound having formula
 $R_1NHCOCH(AR_2)(CH_2)_nCONHOH$ (wherein each of R_1 and R_2 is, substituted or unsubstituted, aryl, cycloalkyl, cycloalkylamino, naphtha, pyridineamino, piperidino, tert-Bu, aryloxy, arylalkyloxy, or pyridine group; wherein A is an amido moiety, O, S, NH, or CH₂; and wherein n is an integer from 3 to 8). The present invention also provides a method of selectively inducing growth arrest, terminal differentiation and/or apoptosis of neoplastic cells and thereby inhibiting proliferation of such cells. Moreover, the present invention provides a method of treating a patient having a tumor characterized by proliferation of neoplastic cells. Lastly, the present invention provides a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically acceptable amount of the compound above. Thus, N-benzoyl-L- α -aminosuberateanilide, i.e. PhCO-Asu-NHPh, was condensed with tert-butylidiphenylsilyloxyamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in CH₂Cl₂ at room temperature for 12 h, followed by deprotection with 5% CF₃CO₂H

in

CH₂Cl₂ for 1.5 h to give PhCO-Asu(NHOH)-NHPh (I). I and PhCH₂O₂C-Asu(NHOH)-NHR (R = quinolin-8-yl) showed activity of murine erythroleukemia cell (MEL) differentiation at 200 and 40 nM, resp., and inhibited histone deacetylase (HDAC) with ID₅₀ of 1 and <10 nM, resp.

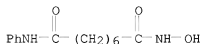
IT 149647-78-9P 329966-65-6P 329966-66-7P
 329966-67-8P 329966-68-9P 329966-69-0P
 329966-77-0P 329966-91-8P 329966-92-9P
 329966-97-4P 329966-98-5P 329967-00-2P
 329967-01-3P 329967-02-4P 329967-03-5P
 329967-19-3P 329967-32-0P 329967-33-1P

329967-35-3P 329967-37-5P 329967-38-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alkanolic acid derivs. as novel class of cytodifferentiating agents and histone deacetylase inhibitors)

RN 149647-78-9 CAPLUS

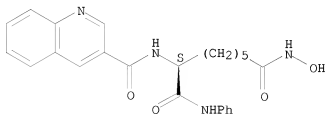
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



RN 329966-65-6 CAPLUS

CN Octanediamide, N8-hydroxy-N1-phenyl-2-[(3-quinolinylcarbonyl)amino]-, (2S)- (CA INDEX NAME)

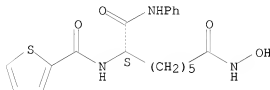
Absolute stereochemistry.



RN 329966-66-7 CAPLUS

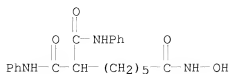
CN Octanediamide, N8-hydroxy-N1-phenyl-2-[(2-thienylcarbonyl)amino]-, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



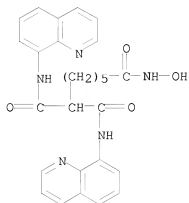
RN 329966-67-8 CAPLUS

CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-diphenyl- (9CI) (CA INDEX NAME)



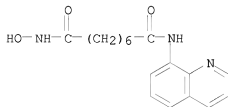
RN 329966-68-9 CAPLUS

CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-di-8-quinolinyl- (9CI) (CA INDEX NAME)



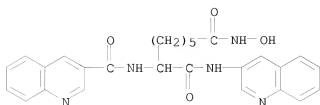
RN 329966-69-0 CAPLUS

CN Octanediamide, N-hydroxy-N'-8-quinolinyl- (9CI) (CA INDEX NAME)



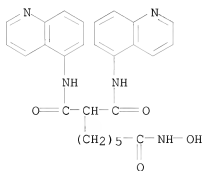
RN 329966-77-0 CAPLUS

CN Octanediamide, N8-hydroxy-N1-3-quinolinyl-2-[(3-quinolinylcarbonyl)amino]- (CA INDEX NAME)



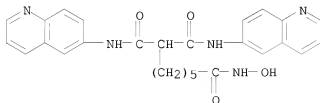
RN 329966-91-8 CAPLUS

CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-di-5-quinolinyl- (9CI) (CA INDEX NAME)



RN 329966-92-9 CAPLUS

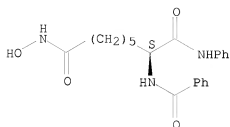
CN 1,1,6-Hexanetricarboxamide, N6-hydroxy-N1,N1'-di-6-quinolinyl- (9CI) (CA INDEX NAME)



RN 329966-97-4 CAPLUS

CN Octanediamide, 2-(benzoylamino)-N8-hydroxy-N1-phenyl-, (2S)- (CA INDEX NAME)

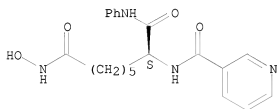
Absolute stereochemistry.



RN 329966-98-5 CAPLUS

CN Octanediamide, N8-(hydroxy-N1-phenyl-2-[(3-pyridinylcarbonyl)amino]-, (2S)-
(CA INDEX NAME)

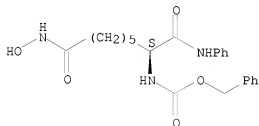
Absolute stereochemistry.



RN 329967-00-2 CAPLUS

CN Carbamic acid, N-[(1S)-7-(hydroxyamino)-7-oxo-1-
[(phenylamino)carbonyl]heptyl]-, phenylmethyl ester (CA INDEX NAME)

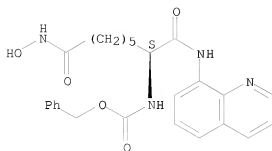
Absolute stereochemistry.



RN 329967-01-3 CAPLUS

CN Carbamic acid, N-[(1S)-7-(hydroxyamino)-7-oxo-1-[(8-
quinolinylamino)carbonyl]heptyl]-, phenylmethyl ester (CA INDEX NAME)

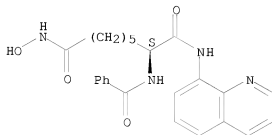
Absolute stereochemistry.



RN 329967-02-4 CAPLUS

CN Octanediamide, 2-(benzoylamino)-N8-hydroxy-N1-8-quinolinyl-, (2S)- (CA INDEX NAME)

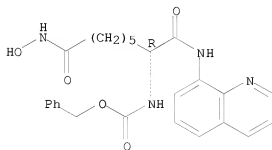
Absolute stereochemistry.



RN 329967-03-5 CAPLUS

CN Carbamic acid, [(1R)-7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

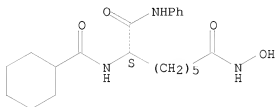


RN 329967-19-3 CAPLUS

CN Octanediamide, 2-[(cyclohexylcarbonyl)amino]-N8-hydroxy-N1-phenyl-, (2S)-

(CA INDEX NAME)

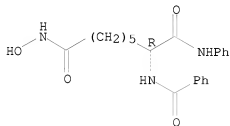
Absolute stereochemistry.



RN 329967-32-0 CAPLUS

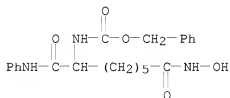
CN Octanediamide, 2-(benzoylamino)-N8-hydroxy-N1-phenyl-, (2R)- (CA INDEX NAME)

Absolute stereochemistry.



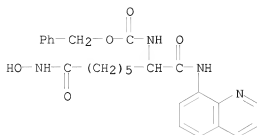
RN 329967-33-1 CAPLUS

CN Carbamic acid, [7-(hydroxyamino)-7-oxo-1-[(phenylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 329967-35-3 CAPLUS

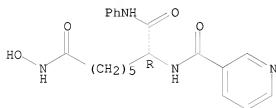
CN Carbamic acid, [7-(hydroxyamino)-7-oxo-1-[(8-quinolinylamino)carbonyl]heptyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 329967-37-5 CAPLUS

CN Octanediamide, N8-hydroxy-N1-phenyl-2-[(3-pyridinylcarbonyl)amino]-, (2R)-
(CA INDEX NAME)

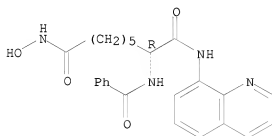
Absolute stereochemistry.



RN 329967-38-6 CAPLUS

CN Octanediamide, 2-(benzoylamino)-N8-hydroxy-N1-8-quinolinyl-, (2R)- (CA
INDEX NAME)

Absolute stereochemistry.



IT 9076-57-7, Histone deacetylase

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
(Miscellaneous); BIOL (Biological study); PROC (Process)(preparation of alkanolic acid derivs. as novel class of cytodifferentiating
agents and histone deacetylase inhibitors)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L42 ANSWER 53 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2001:185791 CAPLUS <LOGINID:20080505>
 DOCUMENT NUMBER: 134:204354
 TITLE: Crystal structure of a histone deacetylase-like protein from Aquifex aeolicus and complexes with inhibitors
 INVENTOR(S): Pavletich, Nikola; Finnin, Michael; Donigian, Jill; Richon, Victoria; Rifkind, Richard A.; Marks, Paul A.; Breslow, Ronald
 PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, USA; Trustees of Columbia University in the City of New York
 SOURCE: PCT Int. Appl., 329 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-----------------|
| WO 2001018045 | A1 | 20010315 | WO 2000-US24700 | 20000908 <-- |
| WO 2001018045 | A9 | 20021107 | | |
| W: CA, JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2383885 | A1 | 20010315 | CA 2000-2383885 | 20000908 <-- |
| EP 1212357 | A1 | 20020612 | EP 2000-968344 | 20000908 <-- |
| EP 1212357 | B1 | 20070502 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY | | | | |
| JP 2003518923 | T | 20030617 | JP 2001-522267 | 20000908 <-- |
| AT 361316 | T | 20070515 | AT 2000-968344 | 20000908 <-- |
| ES 2287033 | T3 | 20071216 | ES 2000-968344 | 20000908 <-- |
| US 20030013176 | A1 | 20030116 | US 2002-95109 | 20020308 <-- |
| US 7124068 | B2 | 20061017 | | |
| US 20070087427 | A1 | 20070419 | US 2006-505214 | 20060816 <-- |
| US 20070100559 | A1 | 20070503 | US 2006-505196 | 20060816 <-- |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1999-152753P | P 19990908 <-- |
| | | | WO 2000-US24700 | W 20000908 <-- |
| | | | US 2002-95109 | A3 20020308 <-- |

AB The present invention provides three-dimensional structural information of the histone deacetylase-like protein (HDLP) from the hyperthermophilic bacterium Aquifex aeolicus. HDLP shares 35.2% amino acid sequence identity with human histone deacetylase (HDAC1). The double mutant C75S/C77S of HDLP is used to facilitate the determination of three-dimensional structure of HDLP bound to a zinc atom at its zinc atom-binding site. The present invention further provides three-dimensional structural information of HDLP double mutant bound by inhibitor mols. (e.g., trichostatin A or suberoyl anilide hydroxamic acid). The three-dimensional structural information of the present invention is useful to design, isolate and screen deacetylase inhibitor compds. capable of inhibiting HDLP, HDAC family members, and HDLP-related mols. The

invention also relates to nucleic acids encoding a mutant HDLP which facilitates the determination of the three-dimensional structure of HDLP in the presence of a zinc atom.

IT 9076-57-7, Histone deacetylase

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(HDAC (histone deacetylase-like protein); crystal structure of a histone deacetylase-like protein from Aquifex aeolicus and complexes with inhibitors)

RN 9076-57-7 CAPLUS

CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 204795-19-7, Histone deacetylase-like protein (Aquifex aeolicus

gene acuC1) 328980-16-1

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; crystal structure of a histone deacetylase-like protein from Aquifex aeolicus and complexes with inhibitors)

RN 204795-19-7 CAPLUS

CN Protein (Aquifex aeolicus gene acuC1 histone deacetylase-like) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 328980-16-1 CAPLUS

CN Histone deacetylase-like protein [75-serine,77-serine] (Aquifex aeolicus gene acuC1) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

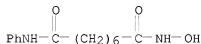
IT 149647-78-9D, complex with deacetylase protein

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(crystal structure of a histone deacetylase-like protein from Aquifex aeolicus and complexes with inhibitors)

RN 149647-78-9 CAPLUS

CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 328980-17-2

RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)

(nucleotide sequence; crystal structure of a histone deacetylase-like protein from Aquifex aeolicus and complexes with inhibitors)

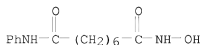
RN 328980-17-2 CAPLUS

CN DNA (Aquifex aeolicus gene acuC1 histone deacetylase-like protein [75-serine,77-serine]-specifying) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 54 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:702583 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 134:272
TITLE: Suberoylanilide hydroxamic acid, an inhibitor of histone deacetylase, suppresses the growth of prostate cancer cells in vitro and in vivo
AUTHOR(S): Butler, Lisa M.; Agus, David B.; Scher, Howard I.; Higgins, Brian; Rose, Adam; Cordon-Cardo, Carlos; Thaler, Howard T.; Rifkind, Richard A.; Marks, Paul A.; Richon, Victoria M.
CORPORATE SOURCE: Cell Biology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SOURCE: Cancer Research (2000), 60(18), 5165-5170
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Suberoylanilide hydroxamic acid (SAHA) is the prototype of a family of hybrid polar compds. that induce growth arrest in transformed cells and show promise for the treatment of cancer. SAHA induces differentiation and/or apoptosis in certain transformed cells in culture and is a potent inhibitor of histone deacetylases. In this study, we examined the effects of SAHA on the growth of human prostate cancer cells in culture and on the growth of the CWR22 human prostate xenograft in nude mice. SAHA suppressed the growth of the LNCaP, PC-3, and TSU-Pr1 cell lines at micromolar concns. (2.5-7.5 μ M). SAHA induced dose-dependent cell death in the LNCaP cells. In mice with transplanted CWR22 human prostate tumors, SAHA (25, 50, and 100 mg/kg/day) caused significant suppression of tumor growth compared with mice receiving vehicle alone; treatment with 50 mg/kg/day resulted in a 97% reduction in the mean final tumor volume compared with controls. At this dose, there was no detectable toxicity as evaluated by weight gain and necropsy examination. Increased accumulation of acetylated core histones was detected in the CWR22 tumors within 6 h of SAHA administration. SAHA induced prostate-specific antigen mRNA expression in CWR22 prostate cancer cells, resulting in higher levels of serum prostate-specific antigen than predicted from tumor volume alone. The results suggest that hydroxamic acid-based hybrid polar compds. inhibit prostate cancer cell growth and may be useful, relatively nontoxic agents for the treatment of prostate carcinoma.
IT 149647-78-9
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(suberoylanilide hydroxamic acid suppresses the growth of prostate cancer cells in vitro and in vivo)
RN 149647-78-9 CAPLUS
CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(suberoylanilide hydroxamic acid suppresses the growth of prostate
cancer cells in vitro and in vivo)
RN 9076-57-7 CAPLUS
CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 55 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:633220 CAPLUS <<LOGINID:20080505>>
DOCUMENT NUMBER: 133:360372
TITLE: Histone deacetylase inhibitor selectively induces
p21WAF1 expression and gene-associated histone
acetylation
AUTHOR(S): Richon, Victoria M.; Sandhoff, Todd W.; Rifkind,
Richard A.; Marks, Paul A.
CORPORATE SOURCE: DeWitt Wallace Research Laboratory, Cell Biology
Program, Memorial Sloan-Kettering Cancer Center and
Graduate School of Medical Sciences of Cornell Medical
School, New York, NY, 10021, USA
SOURCE: Proceedings of the National Academy of Sciences of the
United States of America (2000), 97(18),
10014-10019
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

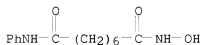
AB Histone deacetylases (HDACs) catalyze the removal of acetyl groups on the
amino-terminal lysine residues of core nucleosomal histones. This
activity is associated generally with transcriptional repression. We have
reported previously that inhibition of HDAC activity by hydroxamic
acid-based hybrid polar compds., such as suberoylanilide hydroxamic acid
(SAHA), induces differentiation and/or apoptosis of transformed cells in
vitro and inhibits tumor growth in vivo. SAHA is a potentially new
therapeutic approach to cancer treatment and is in Phase I clin. trials.
In several tumor cell lines examined, HDAC inhibitors alter the expression
of less than 1% of expressed genes, including the cell cycle kinase
inhibitor p21WAF1. In T24 bladder carcinoma cells, SAHA induces up to a
9-fold increase in p21WAF1 mRNA and protein, which is, at least in part,
because of an increase in the rate of transcription of the gene. SAHA
causes an accumulation of acetylated histones H3 and H4 in total cellular
chromatin by 2 h, which is maintained through 24 h of culture. An
increase in the accumulation of acetylated H3 and H4 was detected
throughout the p21WAF1 promoter and the structural gene after culture with
SAHA. The level of histone acetylation did not change in chromatin
associated with the actin and p27 genes, and their mRNA expression was not
altered during culture of T24 cells with SAHA. Thus, the present findings
indicate that the induction of p21WAF1 by SAHA is regulated, at least in
part, by the degree of acetylation of the gene-associated histones and that
this induced increase in acetylation is gene selective.

IT 9076-57-7, Histone deacetylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
 (inhibition; histone deacetylase inhibitor selectively induces p21WAF1
 expression and gene-associated histone acetylation)
 RN 9076-57-7 CAPLUS
 CN Decacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 149647-78-9
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological
 study); USES (Uses)
 (inhibitor; histone deacetylase inhibitor selectively induces p21WAF1
 expression and gene-associated histone acetylation)
 RN 149647-78-9 CAPLUS
 CN Octanediameide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)

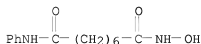


REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 56 OF 56 CAPLUS COPYRIGHT 2008 ACS ON STN
 ACCESSION NUMBER: 2000:277883 CAPLUS <<LOGINID:20080505>>
 DOCUMENT NUMBER: 132:318052
 TITLE: Modulation of gene expression by combination therapy
 with antisense oligonucleotide and gene product
 protein effector
 INVENTOR(S): Besterman, Jeffrey M.; Macleod, Alan Robert; Siders,
 William M.
 PATENT ASSIGNEE(S): Methylgene, Inc., Can.
 SOURCE: PCT Int. Appl., 99 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 2000023112 | A1 | 20000427 | WO 1999-US24278 | 19991019 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW | | | | |
| RW: GH, GN, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2347003 | A1 | 20000427 | CA 1999-2347003 | 19991019 <-- |
| AU 9965194 | A | 20000508 | AU 1999-65194 | 19991019 <-- |
| AU 766084 | B2 | 20031009 | | |

EP 1123111 A1 20010816 EP 1999-953211 19991019 <--
 EP 1123111 B1 20040915
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 JP 2002528391 T 20020903 JP 2000-576885 19991019 <--
 EP 1243289 A2 20020925 EP 2002-14370 19991019 <--
 EP 1243289 A3 20040317
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI, CY
 EP 1243290 A2 20020925 EP 2002-14371 19991019 <--
 EP 1243290 A3 20040317
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI, CY
 AT 275956 T 20041015 AT 1999-953211 19991019 <--
 ES 2228119 T3 20050401 ES 1999-953211 19991019 <--
 US 6953783 B1 20051011 US 1999-420692 19991019 <--
 US 20030096777 A1 20030522 US 2002-145493 20020514 <--
 AU 2004200032 A1 20040129 AU 2004-200032 20040106 <--
 AU 2004200032 B2 20050505
 PRIORITY APPLN. INFO.:
 US 1998-104804P P 19981019 <--
 AU 1999-65194 A3 19991019 <--
 EP 1999-953211 A3 19991019 <--
 US 1999-420692 A3 19991019 <--
 WO 1999-US24278 W 19991019 <--
 AB The invention relates to the modulation of gene expression. In particular, the invention relates to compns. comprising antisense oligonucleotides which inhibit expression of a gene in operable association with protein effectors of a product of that gene, and methods of using the same. In addition, the invention relates to the modulation of mammalian gene expression regulated by methylation.
 IT 149647-78-9
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antisense oligonucleotide and gene product protein effector for gene expression modulation)
 RN 149647-78-9 CAPLUS
 CN Octanediamide, N1-hydroxy-N8-phenyl- (CA INDEX NAME)



IT 9076-57-7, Histone deacetylase
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (antisense oligonucleotide and gene product protein effector for gene expression modulation)
 RN 9076-57-7 CAPLUS
 CN Deacetylase, histone (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

05/05/2008

Print selected from 10-531,754-1.trn

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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